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PSYCHOPHARMACOLOGY ABSTRACTS

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

193140 Buch, H. P.; Schneider-Affeld, F.; Rummel, W.; Knabe, J. Institut fur Pharmakologie and Toxikologie, Universitat des Saarlandes, D-6650 Homburg (Saar), Federal Republic of Germany **Stereochemical dependence of pharmacological activity in a series of optically active N-methylated barbiturates.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 277(2):191-198, 1973.

In a series of N-methylated barbiturates the nature of the cyclic hydrocarbon attached to C-5 does not influence the anesthetic potency ratio of the respective enantiomers. Anesthetic potency of the isomers, however, depends on the length of the aliphatic substituent at C-5. An exchange of methyl versus ethyl at this site causes a shift of the higher anesthetic potency from the (+)-isomer to the (-)-isomer. A further lengthening of the aliphatic substituent at C-5-propyl instead of ethyl in the C-5 phenyl substituted derivative, changes the activity of the (+)-isomer qualitatively to a convulsant. 16 references. (Author abstract)

193278 Muller, W.; Wollert, U. Pharmakolog. Institut der Universitat, D-6500 Mainz, Obere Zahlbacher Str. 67, Germany **Characterization of the binding of benzodiazepines to human serum albumin.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 280(3):229-237, 1973.

The binding of 11 benzodiazepine derivatives to human serum albumin (HSA) is characterized, as determined by means of sephadex gel filtration. Characteristics discussed are: the percentage of bound drug, the binding constants, the number of binding sites per albumin molecule, and the free binding energy. Under the conditions of the experiments, only one binding site of each type exists for all investigated benzodiazepines on the HSA molecule. The affinities of the benzodiazepines to this binding site are different; the part of the benzodiazepine molecule representing the main binding group is identified. 16 references. (Author abstract modified)

193586 Soares, James Ryan. Columbia University **Stereochemical studies on potential central nervous system active agents and studies on the chemistry of some 3-benzoylpiperidines. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-1517 HC$12.50 MF$4.00 184 p.

The four isomers of methyl alpha-phenyl-alpha-(2-piperidyl)-acetate were prepared and their activity as inhibitors of norepinephrine uptake in the peripheral nervous system was evaluated. The (+)-threo-methyl ester hydrochloride was the most active. This isomer and (-)-thiopipradrol hydrochloride, (-)-pipradrol hydrochloride, (-)-desoxyipradrol hydrochloride and (-)-cocaine hydrochloride are the more active antipodes both centrally and peripherally and have identical stereochemical superimposability patterns. The nonasymetric, tricyclic antidepressants such as imipramine and amitriptylene are also superimposable on these more active isomers. Accordingly, various compounds which would be stereochemically superimposable on these were designed and their syntheses undertaken. Specifically, (+)-N-methyl-3- methoxy-3-benzoylpiperidine, (+)-N-methyl-3-acetoxy-3-benzoylpiperidine, (-)-N-methyl-3-benzoylpiperidine, (+)-N,3-dimethyl-3-benzoylpiperidene and (+)-N-methyl-3-ethyl-3-benzoylpiperidine were synthesized, and the reaction between cyanogen bromide and (+)-N-methyl-3-benzoyl-3-hydroxypiperidine under von Braun conditions was investigated and results are reported. (Journal abstract modified)

194148 Muller, W.; Wollert, U. Pharmakologisches Institut der Universitat Mainz, D-6500 Mainz, Obere Zahlbacher Strass 67, Germany **Interactions of benzodiazepines with human serum albumin: circular dichroism studies.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 278(3):301-312, 1973.

The circular dichroism (CD) spectra of 12 benzodiazepine derivatives studied in the presence of human serum albumin are presented. Nearly all substances give biphasic extrinsic Cotton effects. At the CD maxima the molar ellipticities and the anisotropy factors were calculated. The influence of the chemical structure of the benzodiazepines on the induced Cotton effect is discussed. A linear correlation between the anisotropy factors and the logarithms of the partition coefficients of the substances is demonstrated. It is suggested that the phenyl ring of the benzodiazepine molecule is one of the essential groups for the binding of these substances to human serum albumin. 15 references. (Author abstract)

194563 Haya, Katsuji. University of British Columbia, Canada **Thietanes as potential MAO inhibitors and analgetics. (Ph.D. dissertation).** Dissertation Abstracts International. Ottawa, Canada, National Library of Canada, 1973.

Thietanes were investigated as potential monoamine oxidase (MAO) inhibitors. Preliminary experiments indicated that the 3-hydroxyl could be replaced to give 3-amino-2-phenyl thietane, the thietane analog of tranylcypromine desired for MAO inhibition studies. As a possible route to 3-amino-2-phenoxy thietane, several enamines prepared from phenoxy acetaldehyde were subjected to a cycloaddition reaction with methyl sulfene. These results are discussed in relation to the mechanism of the cycloaddition reaction. None of the compounds tested showed significant analgetic activity in an in vitro test based on the inhibition of the contractions of an electrically stimulated guinea pig ileum. The elucidation of the configuration of the synthesized thietanes from their nuclear magnetic resonance spectra and the mass spectral characteristics of thietanes and thietane 1,1-dioxides are discussed in some detail. (Journal abstract modified)

194564 Mizoguchi, Allan H. University of Kansas **Some studies of adrenergic amines: Part I. Role of the aromatic ring in receptor binding. Part II. Beta adrenergic blockade. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-12602 HC$12.50 MF$4.00 136 p.

The importance of pi bonding with the adrenergic receptor and the reason for practolol's cardioselectivity as a beta adrenergic blocking agent were investigated. Analogs of norepinephrine (NE) retaining varying degrees of pi characteristic were sought in the first experiment. The results indicated that the compounds are indirect acting amines, releasing NE from storage vesicles. The results of the regression analysis study in the second experiment indicated that beta blocking potential cannot be correlated with either the lipophilic or electronic contributions of molecular substituents. Therefore, factors important for cardioselectivity likewise cannot be correlated. From pharmacological testing of the mentioned compounds, similar results were obtained. Discrepancies were

observed when trying to correlate cardioselectivity with lipophilicity. (Journal abstract modified)

194565 Reepmeyer, John Charles. University of Kansas **Stereochemical approaches to tricyclic psychoactive agents. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-12618 HC$12.50 MF$4.00 122 p.

Stereochemical approaches to tricyclic psychoactive agents were investigated. In order to define the optimum position of the side chain nitrogen for antidepressant and antipsychotic activity, analogs with sterically rigid side chains were prepared. The addition of 2-chlorothioxanthenyl lithium to 3-dimethylaminocyclohexane followed by dehydration with thionyl chloride and pyridine in dichloromethane gave a mixture of the endocyclic olefin 1a. Following the same procedure using 5H-dibenzo(a,d)cycloheptenyl lithium, a mixture of the endocyclic olefin and the desired exocyclic isomer 1b was obtained. Treatment of the tosyl hydrazone of 10,11-dihydro-5H-dibenzo-(a,d)cyclohepten-5-one with sodium methoxide in pyridine gave the corresponding 5-diazo compound. A benzene solution of the diazo compound was refluxed with N-methylmaleimide to give the spirocyclopropane adduct. Subsequent reduction of the imide with LiAlH4 in ether afforded the desired amine 2a. The chloro-substituted substance 2b was prepared in the same manner. (Journal abstract modified)

195119 Glennon, Richard A. Department of Medicinal Chemistry, School of Pharmacy, SUNY at Buffalo, Buffalo, NY 14214 **A quantum chemical investigation of the pi-electronic structure of the hallucinogenic N,N-dimethyltryptamines.** Research Communications in Chemical Pathology and Pharmacology. 9(1):185-188, 1974.

The quantum chemical investigation of the pi-electronic structure of the hallucinogenic N,N-dimethyltryptamines is discussed. A reexamination of the quantum chemical properties of a series of N,N-dimethyltryptamines indicates that there is no direct relationship between these properties and psychotropic activity. 10 references. (Author abstract)

195238 Atack, Colin; Lindqvist, Margit. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Conjoint native and orthophthaldialdehyde-condensate assays for the fluorimetric determination of 5-hydroxyindoles in brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 279(3):267-284, 1973.

Procedures for the fluorimetric assay of 5-hydroxytryptamine, 5-hydroxytryptophan and 5-hydroxyindole-3-acetic acid in tissues are described. The assay procedures are based both on the native fluorescence of 5-hydroxy-indoles in strong acid and on the considerably higher fluorescence intensity of the fluorophores obtained by means of condensation with orthophthaldialdehyde. A tissue blank procedure, utilizing potassium ferricyanide and cysteine, common to both assays in the joint procedure, is incorporated. The assays have been adjusted to previously described chromatographic procedures, using a strongly acidic cation exchange column, in which these 5-hydroxyindoles and their precursor, tryptophan, and also other biogenic amines and related compounds, are isolated from a single Dowex 50 column. 26 references. (Author abstract modified)

195560 Wolters, Robert J.; Bej, A. J.; Tanner, N. S. Food and Drug Administration, HFD-110, Rockville, MD 20852 **Conformationally constrained analogs of mescaline.** Journal of Pharmaceutical Sciences. 63(9):1379-1382, 1974.

The syntheses of 3-(3,4,5-trimethoxyphenyl)piperidine, 2-(3,4,5-trimethoxybenzyl)piperidine, and 2-(3,4,5-trimethoxyphenyl)morpholine are described. Preliminary pharmacological data comparing these compounds with mescaline are given. 18 references. (Author abstract)

195561 Nelson, Wendel L.; Sherwood, Bob E. Department of Pharmaceutical Sciences, School of Pharmacy, University of Washington, Seattle, WA 98195 **Amphetamine derivatives: 10(e)- and 10(a)-amino-1,2,3,4,4a,9,10,10a- (trans-4a,10a)-octahydrophenanthrene.** Journal of Pharmaceutical Sciences. 63(9):1467-1468, 1974.

Amphetamine analogs (10e)- and 10(a)-amino-1,2,3,4,4a,9,10,10a-(trans-4a,10a)-octahydrophenanthrene, I and II, respectively, were prepared. Hydrogenolysis (methanolic hydrochloric acid) of 9(a)-hydroxy-10(e)-amino-1,2,3,4,4a,9,10,10a-(trans-4a,10a)- octahydrophenanthrene afforded I. A similar procedure for the preparation of II from 9(a)-hydroxy-10(a)-amino-1,2,3,4,4a,9,10,10a-(trans-4a,10a)- octahydrophenanthrene was followed, except the more drastic conditions of a mixture of acetic and perchloric acids were necessary. The compounds were inactive when assayed for amphetamine behavioral and hyperthermia effects. 9 references. (Author abstract)

196252 Daniel, Jimmy Ray. University of Mississippi A **dual study. Part I: synthesis and stereochemistry of some 1-substituted quinolizidines as analogs of biologically active compounds. Part II: amino derivatives of thiophene-fused cyclic ketones as potential CNS. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-1315 HC$12.50 MF$4.00 137 p.

The synthesis and stereochemistry of some 1-substituted quinolizidines as analogs of biologically active compounds are described, and aminoketones derived from thiophene fused cyclic ketones were prepared for their potential central nervous system depressant and antimicrobial properties. The 1(e)-arylquinolizidines and 1(a)-arylquinolizidines were prepared as semirigid analogs of the psychoactive phenethylamines by hydride reduction of the appropriate 1-aryl-4-ketoquinolizidine, and also by hydrogenolysis of 1-aryl-1-hydroxyquinolizidines The semirigid quinolizidine ring was also used to prepare cyclized analogs of the basic anilide analgetics and the local anesthetic, procaine. In preparing aminoketones, the intermediate ketones were prepared in several steps from the appropriate thiophene and converted. Antimicrobial screening showed the highest activity for the bromo and nitro substituted derivatives. Among the organisms used, Candida albicans was the most susceptible. (Journal abstract modified)

196437 Aldous, F. A. B.; Barrass, B. C., Brewster, K.; Buxton, D. A.; Green, D. M.; Pinder, R. M.; Rich, P.; Skeels, M.; Tutt, K. J. Chemical Defence Establishment, Porton Down, Salisbury, Wiltshire, England **Structure-activity relationships in psychotomimetic phenylalkylamines.** Journal of Medicinal Chemistry. 17(10):1100-1111, 1974.

The relationship between the structure of phenylalkylamines and potential correlates of their psychotomimetic activity was studied. Optimum activity is associated with (a) an isopropylamine side chain, with a R-(-) configuration at the carbon atom alpha to the amino group, and (b) 2,5-dimethoxy substitution, together with an alkyl or halo group at position 4 that is probably limited in bulk to n-propyl or bromo. The activity of compounds in producing hyperthermia in rabbits provides good quantitative correlation with reported psychotomimetic activities in man. 36 references. (Author abstract modified)

197279 Bergheim-Irps, E.; Dunges, W.; Heinemann, H. Pharmakologisches Institut der Universitat Mainz, D-65 Mainz, Obere Zahlbacher Strasse 67, Germany **Gas chromatographic analyses of barbiturates in small amounts of blood.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):4, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, a method which allows the analysis of ppM levels of barbiturates in small blood volumes was described. Twenty microliters of blood is extracted with an organic solvent. With the aid of a newly developed microrefluxer the barbituric acids are alkylated, using a new derivatisation method which allows the direct injection of the reaction mixture. Qualitative and quantitative analyses appear to be possible since good recoveries and blank values have been achieved. (Author abstract modified)

197281 Christ, W.; Rakow, D. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, D-1000 Berlin 19, Ulmenallee 30, Germany **A simple and rapid spectrophotometric determination of monoamine oxidase activity.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):R10, 1973

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, a simple and rapid spectrophotometric determination of monoamine oxidase activity was described. The method is based on the high extinction of 4-hydroxy-3-methoxy-benzaldehyde (vanillin) in alkali solution at 345 nm. This product is formed in the course of action of MAO on 4-hydroxy-3-methoxy-benzylamine when used as substrate. Tissues (brain, heart and liver) are homogenized in isotonic KCl. Incubation mixtures consisted of enzyme 4-hydroxy-3-methoxy-benzylamine in a total volume of 5.0ml. Samples were incubated for 30 minutes and the reaction was stopped by the addition of HClO4. 4-Hydroxy-3-methoxy-benzaldehyde formed was extracted into toluene and from toluene reextracted into 1 m K2CO3 solution. The K2CO3 solution was assayed for the product at 345 nm. The reaction was linear with time for at least 50 min and with enzyme concentration over a range of 10-100mg of tissue (brain, heart, liver). (Author abstract modified)

197675 Reisch, J.; Weidmann, K. G.; Triebe, J. Institut fur Pharmazeutische Chemie der Westfalischen Wilhelms-Universitat Munster, D-44 Munster, Germany **/Light induced fragmentation of 3,5-dioxo-1,2-diphenyl-4-n-butylpyrazolidine (phenylbutazone) with nucleophilic agents./** Lichtinduzierte Reaktionen des 4-n-Butyl-1,2-diphenylpyrazolidin-3,5-dion (Phenylbutazon) mit nucleophilen Agentien. Experientia (Basel). 30(5):451-452, 1974.

The light induced fragmentation of 3,5-dioxo-1,2 diphenyl-4-n-butylpyrazolidine (phenylbutazone) is described. In the presence of protonic, nucleophilic agents, the C-N bond of the intermediate aziridinone is split. Subsequent fragmentation products are illustrated. 8 references. (Journal abstract modified)

197923 Swett, Chester, Jr. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Rd., Waltham, MS 02154 **Adverse reactions to chlorpromazine in psychiatric patients.** Diseases of the Nervous System. 35(11):509-511, 1974.

In 470 consecutively monitored psychiatric inpatients who received chlorpromazine, adverse reactions attributed to the drug were reported in 150 (31.9%). The reaction was considered life-threatening in three patients. Findings indicate that reactions are more frequent with higher daily doses and the intramuscular route was associated with earlier onset of a reaction. 8 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

193279 Rubio, M. C.; Langer, S. Z. Consejo Nacional de Investigaciones, Cientificas y Tecnicas, Junin 956 - 5 piso, Buenos Aires, Argentina **Effects of the noradrenaline metabolites on tyrosine hydroxylase activity in guinea-pig atria.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 280(3):315-330, 1973.

The effects of noradrenaline, its five metabolites, and metanephrine, on tyrosine hydroxylase activity in guinea pig atria were examined and the potency of noradrenaline is noted. The effect of normetanephrine in the intact tissue is related to the ability of this compound to release endogenous noradrenaline. A reserpine like agent, Ro 4-1284, was not found to inhibit tyrosine hydroxylase activity in the homogenate but in the intact tissue the inhibition was more than 50%. This effect of Ro 4-1284 in the intact tissue appears to be related to the releasing effects of this agent and to an increase in the axoplasmic levels of 3,4-dihydroxyphenylglycol (DOPEG). Since the formation of DOPEG represents the main metabolic pathway for the neurotransmitter in adrenergic nerve endings, the results are compatible with the view that the cytoplasmic concentration of DOPEG could also participate in the regulation of the activity of tyrosine hydroxylase, in addition to the pool of extravesicular noradrenaline. 24 references. (Author abstract modified)

195092 Fuller, R. W.; Perry, K. W.; Wong, D. T.; Molloy, B. B. Lilly Research Laboratories, Eli Lilly & Company, Indianapolis, IN 46206 **Effects of some homologues of 4-chloroamphetamine on brain serotonin metabolism.** Neuropharmacology (Oxford). 13(7):609-614, 1974.

The effects of some homologues of 4-chloroamphetamine on brain serotonin metabolism were examined. Three homologues of 4-chloroamphetamine, with longer or shorter side chains, had different effects on rat brain serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) levels than did 4-chloroamphetamine itself. Shortening the side chain greatly diminished the activity of 4-chloroamphetamine on 5-hydroxyindole metabolism; 4-chloro-alpha-methylbenzylamine had little effect on 5-HT or 5-HIAA levels in vivo or on 5-HT uptake into synaptosomes or oxidation by monoamine oxidase in vitro. Lengthening the side chain abolished depletion of brain 5-HT by 4-chloroamphetamine but not the ability to affect 5-HT uptake and metabolism. Both of the longer homologues antagonized the depletion of brain 5-HT by 4-chloroamphetamine, a further indication that they block uptake by 5-HT neurons in vivo. These results indicate that the depleting action of 4-chloroamphetamine on brain 5-HT is lost by altering the side chain but that other actions of 4-chloroamphetamine on brain 5-HT metabolism are retained in the longer side chain homologues. 15 references. (Author abstract modified)

196444 Hamanka, Toshinori; Ishii, Makoto; Nishizaki, Hiroyuki; Suga, Toshio. Koganei Research Laboratory, Tobishi Pharmaceutical Co., Ltd., Koganei, Tokyo, Japan **Pharmacology of magnesium glutamate hydrobromide (PS-042), a new tranquilizer: third part, psychopharmacological studies.** Journal of the Medical Society of Toho University (Tokyo). 20(5/6):663-680, 1973.

The effects of magnesium glutamate hydrobromide (PS-042) were observed in various laboratory animals. When injected into rats (200mg/kg ip), PS-042 induced stretching, tachycardia, and lethargy. A larger dose (500mg/kg ip) induced stretching, unsteady posture, and abnormality in walking. Cats showed light sleep behavior at low dosages (50 or 100mg/kg ip) and unsteady landing behavior and vomiting at a higher dosage (200mg/kg). No significant inhibition of response to electric shock was observed in cats. In dogs, 100mg/kg injections induced vomiting. High amplitude, slow wave EEG's were observed after large dosages in rats. 8 references.

198055 Sanghvi, I.; Gershon, S. Psychopharmacology Research Unit, Dept. of Psychiatry, New York Univ. Medical Center, New York, NY **Evaluation of clinical prediction of antidepressant activity using various animal test models.** Psychopharmacology Bulletin. 10(2):20-22, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which describes the major groups of test models used for evaluating drug antidepressant activity. The six major groups of tests were: antagonism of the effects of reserpine like drugs; potentiation of phenethylamines; effects on the autonomic nervous system; inhibition of norepinephrine uptake and release; monoamine oxidase inhibition; and antagonism of muricide behavior in rats. 22 references. (Journal abstract modified)

198057 Weissman, Albert. Department of Pharmacology, Pfizer, Inc., Groton, CT **The use of drug interactions in animals for selecting psychotropic drugs.** Psychopharmacology Bulletin. 10(2):23-24, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which identified 'simple drug interaction studies.'Criteria in selecting examples include: simplicity of drug treatment; convenience of species; and simplicity of the endpoint. Judicious interaction procedures to identify exploratory CNS agents were described. 1 reference. (Journal abstract modified)

198058 Free, S. M., Jr. Smith, Kline, & French Laboratories, Philadelphia, PA **Multi-dimensional scaling to relate animal pharmacology and clinical symptoms of psychopharmacologic agents.** Psychopharmacology Bulletin. 10(2):25, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which described animal pharmacology profiles and clinical profiles for 11 compounds. ED50's signs of activity, inactive responses, and some guesses where the test had not been performed were plotted for animal trials on the two dimensions of antipsychotic - antidepressant activity and tranquilizer - nontranquilizer activity for each compound. Compounds were also rated for relative activity on certain animal pharmacology tests, and tests were rated on the relative sensitivity of their discrimination between drugs. Clinical symptoms as measured by the Brief Psychiatric Rating Scale and the Factor Construct Rating Scale were plotted in a similar manner and the three plots showed significant correlation. A similar study was conducted using only antidepressants. (Journal abstract modified)

198059 Overall, John E. University of Texas Medical Branch, Galveston, TX **An extension of multidimensional scaling to facilitate clinical interpretation of animal test models.** Psychopharmacology Bulletin. 10(2):25-27, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which extended multidimensional scaling to facilitate clinical interpretation of animal test models. A computer program was written to accomplish a multidimensional scaling analysis based on one multivariate data set and then to mathematically relate variables in another multivariate data set to the derived scale dimensions. The program is used to position several different sets of clinical vectors in the same animal test space. An alternate application involves the development of a scale model on the basis of relationships among symptom profiles for patients who are selected for treatment with various drugs, and its projection into the model animal test vectors. (Journal abstract modified)

198072 Simpson, George M. Rockland State Hospital, Orangeburg, NY **Drug-screening program for drug-resistant schizophrenics.** Psychopharmacology Bulletin. 10(2):52-53, 1974.

New antischizophrenic compounds are evaluated clinically with emphasis on side-effects and physiological parameters and existing psychopharmacological procedures are improved. Chronic schizophrenics between the ages of 18 and 60 were free of medication for 1 month and then treated for 3 months with one of the following agents: metiapine, GPA 1714, milipertine, naranol, loxapine imipramine, chlorpromazine, (Thorazine) butaperazine, lithium, and various antidepressants. (Journal abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

192925 Jakupcevic, M.; Lackovic, Z.; Damjanov, I.; Bulat, M. Laboratory for Experimental Neuropathology, Dept. of Biology, Institute R. Boskovic, 41001 Zagreb, Yugoslavia **Biogenic amines in a retransplantable neurogenic teratocarcinoma.** Experientia (Basel). 30(6):652-653, 1974.

An analysis of the neurogenic teratocarcinomas for their content of biogenic amines, known to have a specific role in neurotransmission, was made in mice to gain insight into the functional status of the tumor. Tumor bearing mice were sacrificed and determinations were made of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA). Results show that the tumors examined contained 5-HT and 5-HIAA in amounts comparable or higher than those measured in normal mouse brains. There was more variation in the content of these substances in tumors than in the brains. The tumors did not contain noradrenaline and dopamine in measurable amounts. Treatment of tumor bearing animals with trancylpromine caused an increase of 5-HT in tumors for 29% and a decrease of 5-HIAA for 60% in relation to control values. Injection of probenecid to tumor bearing animals caused no detectable increase in the content of 5-HIAA in the tumors. 7 references.

192933 Burkard, W. P.; Bartholini, G. Dept. of Experimental Medicine, F. Hoffmann-La Roche and Co. Ltd., 4002 Basel, Switzerland **Changes in activation of adenylate cyclase and of dopamine turnover in rat striatum during prolonged haloperidol treatment.** Experientia (Basel). 30(6):685, 1974.

At the Sixth Annual Meeting of the Union of Swiss Societies for Experimental Biology changes in the activation of adenylate cyclase and of dopamine (DA) turnover in rat striatum during prolonged haloperidol treatment were reported. A progressive enhancement of the activation of striatal adenylate cyclase by DA was observed in rats treated for 1 to 21 days with haloperidol. The increase in striatal homovanillic acid caused by neuroleptic agents probably indicates a compensatory feedback activation of DA neurons triggered by the

blockade of DA receptors. It was suggested that the enhanced effect of DA on striatal adenylate cyclase during prolonged haloperidol treatment reflects a supersensitivity of DA receptors which might be responsible for the reduction of the feedback activation of the dopaminergic neurons. (Journal abstract modified)

192936 Bucher, M.-B.; Schorderet, M. Institut de Pharmacologie, Ecole de Medicine, 20, rue de l'Ecole-de-Medecine, 1211 Geneva 4, Switzerland **Selective stimulation by dopamine of adenylate cyclase in homogenates of rabbit retina.** Experientia (Basel). 30(6):694, 1974.

At the Sixth Annual Meeting of the Union of Swiss Societies for Experimental Biology, selective stimulation by dopamine of adenylate cyclase activity (ACA) in homogenates of rabbit retina was reported. Homogenates were assayed for ACA in a medium containing tris-hydrochloric acid, ATP, magnesium ion, sodium chloride, potassium chloride, EGTA and theophylline in optimal concentrations. The cyclic-AMP (CAMP) formed was extracted and measured. The rate of formation of CAMP was a function of time and amount of protein. Dopamine was found to be the most potent activator of the enzyme. The effect of dopamine was blocked by haloperidol. Apomorphine caused a 49% increase in ACA. Noradrenaline stimulated ACA but isoproterenol or phenylephrine had no effect. The results suggest that homogenates of rabbit retina be used to study dopamine stimulated ACA and possibly dopamine receptors. (Journal abstract modified)

192937 Delini-Stula, A. Research Dept., Pharmaceuticals Div., CIBA-GEIGY Ltd., 4000 Basel, Switzerland **Suppression of conditioned hyperthermic response by l- and D-oxprenolol in rats.** Experientia (Basel). 30(6):695, 1974.

At the Sixth Annual Meeting of the Union of Swiss Societies for Experimental Biology, the suppression of conditioned hyperthermic responses by l-oxoprenolol and d-oxprenolol in rats was discussed. Repeated administration of the two drugs to rats subjected to a conditioning procedure was found to prevent the development of conditioned hyperthermia. d-Oxprenolol was more effective in this respect than l-oxprenolol. The acquisition of conditioned avoidance behavior was not affected by the drugs. Towards the end of the experiment, learning failures increased slightly. Observed effects could not be ascribed to the peripheral beta blocking action of the drugs. The attenuation of fear in a stressful situation was suggested as a possible mode of action. (Journal abstract modified)

192940 Pieri, L.; Pieri, M. Dept. of Experimental Medicine, F. Hoffmann-La Roche and Co. Ltd., Grenzacherstrasse 124, CH-4002 Basel, Switzerland **Drug-induced rotation in rats after unilateral intracerebral injection of 5,6-dihydroxytryptamine (5,6-HT).** Experientia (Basel). 30(6):696-697, 1974.

At the Sixth Annual Meeting of the Union of Swiss Societies for Experimental Biology, drug induced rotation in rats after unilateral intracerebral injection of 5,6-dihydroxytryptamine (5,6-HT) was reported. In 5,6-HT lesioned rats, apomorphine induced rotation towards the nonlesioned side whereas d-methamphetamine evoked ipsilateral rotation. Haloperidol blocked the effect of apomorphine and d-methamphetamine. LSD elicited controlateral rotation; mescaline proved inactive; haloperidol blocked the rotation induced by LSD. It was concluded that LSD may exert an apomorphine like direct stimulation of dopamine receptors. (Journal abstract modified)

192944 Lorez, H. P.; Saner, A. Dept. of Experimental Medicine, F. Hoffmann-La Roche and Co. Ltd., 4002 Basel, Switzerland **D,L-p-Chloro-N-methylamphetamine (P) induced accumulation of 5-HT in nonterminal axons.** Experientia (Basel). 30(6):706, 1974.

At the Sixth Annual Meeting of the Union of Swiss Societies for Experimental Biology, d,l-p-chloro-N-methylamphetamine (P) induced accumulation of 5-hydroxytryptamine (5-HT) in nonterminal axons of the rat was reported. An indolamine (IA) depletion in the terminal axons was observed after standard P treatment of rats. In nonterminal axons of median forebrain bundle, an IA accumulation was present. Moderate yellow formaldehyde induced fluorescence (FIF) occurred in nonterminal axons 1-6 days after P. the FIF was abolished by reserpine but intensified by nialamide and by reserpine plus nialamide in P pretreated rats. The data indicated that the accumulated FIF represented 5-HT. Thus P treatment may be used for mapping 5-HT pathways. (Journal abstract modified)

193050 Cuello, A. C.; Shoemaker, W. J.; Ganong, W. F. Facultad de Farmacia y Bioquimica, Universidad Nacional de Buenos Aires, Junin 956, Buenos Aires, Argentina **Effect of 6-hydroxydopamine on hypothalamic norepinephrine and dopamine content, ultrastructure of the median eminence, and plasma corticosterone.** Brain Research (Amsterdam). 78(1):57-69, 1974.

The effects of 6-hydroxydopamine on the catecholamine content of the hypothalamus and other tissues, the morphology of the median eminence of the hypothalamus, and plasma corticosterone were studied after injection of the drug. Both intraperitoneal and intraventricular administration of 6-hydroxydopamine led to a decrease in hypothalamic norepinephrine concentration and to destructive changes in some of the neurons ending in the external layer of the median eminence without destruction of neighboring neurons. Fifteen days after injection, hypothalamic norepinephrine and plasma corticosterone had returned to normal in animals given 6-hydroxydopamine intraperitoneally. In rats injected intraventricularly, hypothalamic norepinephrine was still reduced but plasma corticosterone was normal. In both groups at 15 days, neuronal debris had accumulated in phagocytic cells, but most neurons appeared normal. Data indicate that norepinephrine containing neurons end in the external layer of the median eminence. 24 references. (Author abstract modified)

193139 Guimaraes, S.; Brandao, F. Laboratorio de Farmacologia, Faculdade de Medicina, Porto, Portugal **Comparison between the effects produced by chronic denervation and by cocaine on the sensitivity to, and on the disposition of, noradrenaline in isolated spleen strips.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 277(2):163-174, 1973.

The influence of cocaine and of chronic denervation on sensitivity and rate of inactivation of noradrenaline and the role played by iproniazid and tropolone under both conditions was studied on isolated strips of cat spleen. The oil immersion technique was used to study the rate of inactivation of noradrenaline. Cocaine was used in four different concentrations and in all it enhanced the sensitivity to noradrenaline. Since denervation produces an enhancement of the effect of noradrenaline smaller than that caused by cocaine, the blockade of neuronal uptake cannot fully account for all supersensitivity induced by cocaine. Cocaine produces no further enhancement of the effect of noradrenaline in denervated strips. The influence of cocaine and denervation on the role played by iproniazid and tropolone on the inactivation of

noradrenaline was not significantly different. 31 references. (Author abstract modified)

193301 Neuvonen, P. J.; Westermann, E. Institut fur Pharmakologie, Medizininsche Hochschule Hannover, D-3000 Hannover-Kleefeld, Karl Wiechert-Allee 9, Germany **Studies on some metabolic effects of dopa and dopamine in the rat.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 284(2):115-131, 1974.

Metabolic effects of L-dopa and dopamine were compared with those of noradrenaline, adrenaline and tyramine by measuring the changes of plasma free fatty acids (FFA), plasma glycerol and plasma glucose as well as those of blood lactate and blood pyruvate in male rats. Pretreatment of the animals with phentolamine prevented the hyperglycemic response to dopamine or noradrenaline without clearcut effects on the lipolytic effect of these catecholamines. Pretreatment with dihydroergotamine antagonized the hyperglycemic effect of adrenaline and prevented that of dopamine and noradrenaline, while the effect of catecholamines on plasma glycerol concentration was not affected. The elevation in plasma FFA level induced by catecholamines was clearly antagonized by dihydroergotamine. Effects of pargyline, 6-hydroxydopamine, and syrosingopine are also reported. Since the metabolic effects of dopamine were clearly antagonized by various alpha-receptor and beta-receptor blocking agents and by chemical sympathectomy, it is concluded that dopamine exerts its metabolic effects through a stimulation of alpha-adrenoceptors and beta-adrenoceptors and that part of these effects is mediated by a tyramine like action of dopamine. 34 references. (Author abstract modified)

193302 Kehr, Wolfgang. Dept. of Pharmacology, Fack, S-40033, Goteborg 33, Sweden **A method for the isolation and determination of 3-methoxytyramine in brain tissue.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(2):149-158, 1974.

A method for the chromatographic separation and fluorimetric determination of 3-methoxytyramine in brain tissue is described. The chromatographic procedure is an extension of the method for the separation of noradrenaline, dopamine and 5-hydroxytryptamine published by Atack and Magnusson (1970) and can be combined with that for monoamine precursors described by Kehr et al. (1972). The level of 3-methoxytyramine found in normal rat brain is below the limit of sensitivity. The amount of 3-methoxytyramine accumulating after inhibition of monoamine oxidase (MAO) differs depending on the inhibitor used. These differences in 3-methoxytyramine formation might be due to incomplete MAO inhibition, changes in dopamine synthesis, and releasing activity of the compounds investigated. 17 references. (Author abstract modified)

193303 Liebman, Jeffrey M.; Butcher, Larry L. Dept. of Psychiatry, School of Medicine, University of California, La Jolla, CA 92037 **Comparative involvement of dopamine and noradrenaline in rate-free self-stimulation in substantia nigra, lateral hypothalamus, and mesencephalic central gray.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 284(2):167-194, 1974.

The effects of self-stimulation (SS) of several drugs (pimozide, apomorphine, D-amphetamine, and L-amphetamine) having dissimilar effects on central dopaminergic and noradrenergic neurotransmission were examined in Sprague-Dawley albino rats. The effects on Ss of these agents in lateral hypothalamus (HL) and substantia nigra (SN) were separately determined. A rate free test of SS was employed. The existence of a dopaminergic substrate of SS in SN is confirmed, but HL SS was also reduced by pimozide. Low doses of apomorphine elevated SS in HL while not influencing or slightly reducing SS in SN. Higher doses of apomorphine reduced SS in both regions. The enhancing effect of 0.1mg/kg D-amphetamine on SS was greater in HL than in SN. However, D-amphetamine tended to increase Ss more strongly than did L-amphetamine in SN as well as HL. It is concluded that HL SS may be mediated by both noradrenergic and dopaminergic substrates. The possibility of noradrenergic or dopaminergic mediation of SS in other brain regions is also investigated. 35 references. (Author abstract modified)

193304 Smith, R. D.; Breese, G. R.; Mueller, R. A. Dept. of Pharmacology, Univ. of North Carolina School of Medicine, Chapel Hill, NC 27514 **Potentiation of drug-initiated adrenal tyrosine hydroxylase induction by diazepam.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 284(2):195-206, 1974.

Effects of the administration of diazepam in further increasing in vitro adrenal tyrosine hydroxylase (TH) activity caused by drugs which produce an increase in preganglionic nerve activity as a result of actions outside the central nervous system in rats are reported. Adrenal enzyme induction provoked by isoproterenol and 6-hydroxydopamine was increased by diazepam administration, whereas that produced by reserpine or insulin was not altered. The enhanced adrenal TH activity produced by diazepam pretreatment and isoproterenol administration could not be attributed to an increase in intensity or to an altered body temeperature. Administration of 5-hydroxtryptophan did not block the TH induction produced by concurrent administration of diazepam and isoproterenol. The effect of diazepam on adrenal TH induction may be the result of its ability to interfere with central nervous system amine containing nerve functions which modulate preganglionic nerve activity, but the particular neurotransmitter system involved has not been determined. 35 references. (Author abstract modified)

193419 Lewis, S. C.; Brown, D. J.; Forney, R. B. Dept. of Toxicology, Indiana Univ. School of Medicine, Indianapolis, IN **Absence of tolerance to the hypotensive effects of delta9-tetrahydrocannabinol in hypertensive rats.** Toxicology and Applied Pharmacology. 29(1):78, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology in March, 1974, an investigation of the development of tolerance to the hypotensive effects of repeated low to moderate doses of tetrahydrocannabinol (THC) was reported for rats. THC was administered ip to spontaneously hypertensive rats (SHR) in a corn oil vehicle and blood pressure was measured. Controls were administered vehicle alone. Results indicate that SHR did not become tolerant to the hypotensive effects of delta9-THC when administered as described. (Journal abstract modified)

193421 Alleva, John J.; Waleski, Mary V.; Alleva, Frederic R.; Balazs, Tibor. Food and Drug Administration, Washington, DC **Effect of single and daily injections of phenobarbital on ovulation in hamsters.** Toxicology and Applied Pharmacology. 29(1):110, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology in March, 1974, the effects of acute and chronic injections of phenobarbital on the central mechanism that controls pituitary gonadotropins (PG) in the hamster was reported. Ovulation occurred normally every fourth day between 0100h and 0300h. In both studies, the initial blockage of ovulation was successful at first but later the normal 4 day vaginal

cyclicity returned. Two weeks after the chronic study ended, injection of one group on day three was effective again and one given earlier than usual on day four also blocked PG release. It was concluded that the eventual failure of the daily injections to block PG release was a result of a change in the central mechanism. (Journal abstract modified)

193422 Proctor, C. D.; Cho, J. B. Meharry Medical College, Nashville, TN **Phenothiazine tranquilizer PD-50's exerted against amphetamine effect in aggregated mice.** Toxicology and Applied Pharmacology. 29(1):115-116, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the median protective doses (PD-50's) exerted by phenothiazine tranquilizers against a 100% lethal dose of dl-amphetamine in aggregated mice were shown to be useful screening models in predicting the approximate rank order potency of these tranquilizers. After ip injection of the amphetamine the mice were aggregated and observed over 4 hours for lethality. Measurement of PD-50's demonstrated that the descending order of protective potency for the tranquilizers tested is: fluphenazine, perphenazine, thiopropazate, chloropromazine, thioridazine, promazine. The protection afforded was effected without marked neurological deficit in the mice. (Journal abstract modified)

193423 Blackshear, M. A.; Harris, M. L.; Bennett, R.; Proctor, C. D. Meharry Medical College, Nashville, TN **An effect of amphetamine on mouse brain polyribosomes.** Toxicology and Applied Pharmacology. 29(1):116, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the effect of dl-amphetamine on brain polyribosome aggregation was reported in adult albino mice examined at 30 min postinjection. Results indicate that dl-amphetamine is capable of causing disaggregation of heavy polyribosomes into lighter polyribosomes in mouse brain. The effect was more marked in crowded mice given dl-amphetamine than it was in mice kept in solitary state after amphetamine administration. (Journal abstract modified)

193424 Harris, M. L.; Blackshear, M. A.; Bennett, R.; Proctor, C. D. Meharry Medical College, Nashville, TN **An effect of amphetamine on incorporation of leucine into mouse brain protein.** Toxicology and Applied Pharmacology. 29(1):116-117, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the effect of amphetamine on the incorporation of leucine into mouse brain protein was reported. Employing (UL-14C)l-leucine, incorporation of leucine into protein was studied in various fractions of the fractionated polyribosomes. The results show a decreased incorporation of leucine into brain protein caused by the dl-amphetamine, an effect which parallels the decrease in heavy polyribosomes induced by the amphetamine. The action of the amphetamine was more marked in crowded mice than in mice solitary confined. (Journal abstract modified)

193425 Hitner, H.; DiGregorio, G. J. Dept. of Pharmacology, Hahnemann Medical College, Philadelphia, PA **Mechanism of action of phencyclidine on the peripheral sympathetic nervous system.** Toxicology and Applied Pharmacology. 29(1):117, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the mechanism of action of phencyclidine (PCP) on the peripheral nervous system was reviewed. PCP produced pressor responses in rats and cats and potentiated the pressor responses to norepinephrine (NE). PCT potentiated NE induced contractions in the guinea pig vas deferens while completely blocking acetylcholine induced contractions. PCP potentiated both electrical and epinephrine (EP) induced contractions on the in vivo cat nictitating membrane preparation. Studies on the compound action potentials of the frog sciatic nerve indicate that PCP has a local anesthetic action and at lower concentrations PCP facilitates nerve conduction causing a rise in the height of the action potential. It appears that the mechanism of action of PCP might involve an ion effect related to either sodium or calcium ion. (Journal abstract modified)

193426 Cohn, M. L.; Kraynack, B. J.; Cohn, M. Univ. of Pittsburgh School of Medicine, Pittsburgh, PA **Antianesthetic effects of cyclic AMP and analeptic drugs as determined by reversal of amobarbital-induced narcosis.** Toxicology and Applied Pharmacology. 29(1):117, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the antianesthetic effects of dibutyryl cyclic-AMP and analeptic drugs, picrotoxin, d-amphetamine, pentylenetetrazal, caffeine, theophylline, strychnine, methylphenidate and doxapram were compared in the rat. Only dibutyryl cyclic-AMP and picrotoxin administered intracerebroventricularly shortened the duration of amobarbital induced narcosis. None of the other analeptic drugs administered demonstrated any antianesthetic properties. Patients suffering from drug overdosage should not be treated with these analeptic drugs because the therapy may add to the toxicity already present. It was shown in rats and squirrel monkeys that, due in part to its effective antianesthetic action, dibutyryl cyclic-AMP is an effective antidote to barbiturate overdosage. (Journal abstract modified)

193428 Wagner, Steven R.; Greene, Frank E. Dept. of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State Univ. College of Medicine, Hershey, PA **Effect of acute and chronic dieldrin exposure on brain biogenic amines of male and female rats.** Toxicology and Applied Pharmacology. 29(1):119-120, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, acute and chronic studies of the possible effects of dieldrin on brain concentrations of norepinephrine (NE), dopamine (DA) and serotonin (5-HT) were reported. Adult male and female rats were studied to determine if brain concentrations of the biogenic amines were affected and if sex differences were apparent. Five h after an oral dose of dieldrin severe neurotoxic signs were observed, especially in the male rat. Results indicate that dieldrin is capable of altering brain tissue concentrations of NE, DA and 5-HT under certain conditions and that sex differences are minimal. (Journal abstract modified)

193429 Smith, S.; Kennedy, G. L.; Keplinger, M. L.; Calandra, J. C.; Nuite, J. A. Industrial BIO-TEST Laboratories, Inc., Northbrook, IL **Teratologic and reproduction studies with cyclazocine.** Toxicology and Applied Pharmacology. 29(1):124, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the effects of cyclazocine on embryo and fetal development, and fertility and reproduction in the rat were reported. Food consumption, behavior and mating and fertility indexes were similar for control and treated groups. The teratogenic potential was studied in rats and rabbits. Findings indicate that cyclazocine has no effect on fertility and reproduction in rats and is not teratogenic to rats and rabbits. (Journal abstract modified)

193447 Harvey, Alan L.; Dryden, William F. Department of Physiology and Pharmacology, University of Strathcylde, George St., Glasgow, G1 1XW, Scotland **Depolarization, desensitization and the effects of tubocurarine and neostigmine in cultured skeletal muscle.** European Journal of Pharmacology (Amsterdam). 27(1):5-13, 1974.

The actions of acetylcholine, carbachol, d-tubocurarine and neostigmine were studied in cultures of chick embryo muscle. Both agonists produced a rapid, concentration dependent depolarization. The depolarization to a given concentration was greater in older cells with higher resting membrane potentials, but the response percent of resting potential was constant throughout development. Despite continued presence of the agonists, depolarization was not maintained, the membrane potential returning to control level in about 15 minutes. The rate of recovery increased with age of cells and concentration of agonist. Specific desensitization of acetylcholine receptors was demonstrated. Cross-desensitization between acetylcholine and carbachol was observed, but receptor desensitization was unaffected by potassium induced desensitization. d-Tubocurarine competitively antagonized the cholinomimetic response. Neostigmine did not potentiate responses to low concentrations of acetylcholine, but did, itself, cause some desensitization. The results indicate that the acetylcholine receptors of cultured skeletal muscle are similar in many respects to adult nicotinic receptors. 28 references. (Author abstract)

193448 Kelly, Deirdre M.; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, 7, Yorkshire, England **Mechanisms of tremor induction by harmine.** European Journal of Pharmacology (Amsterdam). 27(1):14-24, 1974.

Various agents known to modify cerebral serotoninergic, dopaminergic and cholinergic function were used to investigate the possible relationship between these transmitter systems and the induction and modulation of harmine tremor in rats. The results indicate a noninvolvement of cerebral cholinergic function and a possible involvement of cerebral serotoninergic and/or dopaminergic function with harmine tremor. Anticholinergic agents like atropine failed to modify tremor; dopamine agonists, like L-dopa reduced tremor, and monoamine depleting agents such as reserpine enhanced tremor. Modification of harmine tremor by a serotonin agonist or antagonist (5-hydroxytryptophan, p-chlorophenylalanine) was difficult to assess, but, nevertheless, it was considered that increased cerebral serotonin levels would enhance harmine tremor. The results are discussed in the light of evidence that, while dopamine agonists are effective in reducing Parkinsonian tremor, the same agents will also reduce harmine tremor. 44 references. (Author abstract)

193449 Segal, Mark. Department of Psychiatry, Hadassah Medical Organization, P.O. Box 499, Jerusalem, Israel **Central implantation of cannabinoids: induction of epileptiform discharges.** European Journal of Pharmacology (Amsterdam). 27(1):40-45, 1974.

Intracerebral (i.c.)implants of delta9-tetrahydrocannabinol (delta9-THC) and delta8-tetrahydrocannabinol (delta8-THC), cannabidiol and the 11-hydroxy-metabolite of delta8-THC induced qualitatively similar alterations in the electroencephalographic pattern of rabbit brain. The doses of delta9-THC and delta8-THC required to induce these alterations were equivalent; that of the 11-hydroxy-metabolite of delta8-THC was substantially lower, while that of cannabidiol was substantially higher. Although the convulsant effects obtained upon i.c. implantation were reproducible, it is too soon to assess this effect in relation to THC's central effects in man. One of the main reasons for this is that the convulsant effect could only be sporadically produced by the i.v. injection of large quantities of delta8-THC in the rabbit. Consideration is given to the possiblity that the 11-hydroxy-metabolite of delta8-THC is the active form of its parent compound in rabbit brain. 17 references. (Author abstract)

193450 Costall, Brenda; Naylor, Robert J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, 7, Yorkshire, England **Mesolimbic involvement with behavioural effects indicating antipsychotic activity.** European Journal of Pharmacology (Amsterdam). 27(1):46-58, 1974.

The bilateral electrolytic brain lesion technique was used in rats to determine the role of the nucleus accumbens septi (ACB), nucleus interstitialis stria terminalis (ST) and the tuberculum olfactorium (TUO), areas of the dopaminergic mesolimbic system, in the mediation of the cataleptic and antistereotypic effects of neuroleptic and nonneuroleptic agents. The cataleptic action of all agents tested, excepting morphine and RS 86, was reduced by lesions of the ACB. Lesions of the ST similarily reduced the action of certain agents and also abolished the ability of neuroleptic and cholinergic agents to synergize in the production of catalepsy. Ablation of the TUO did not modify the cataleptic action of any agent tested. Lesions of the ST reduced the antistereotypic activities of all neuroleptic and nonneuroleptic agents tested, with the exception of oxypertine. Lesions of the ACB or TUO reduced the antistereotypic activities of all agents excepting RS 86. The results indicate a differential involvement of mesolimbic areas with the behavioral effects of catalepsy and stereotypy antagonism which are used as experimental indicators of antipsychotic activity. However, the relationship of mesolimbic function to antipsychotic activity is questioned because of the involvement of this area with action of nonneuroleptic agents. 26 references. (Author abstract modified)

193451 Jacob, Joseph J.; Girault, Jeanne-Marie T. Laboratory of Pharmacology and Toxicology, Pasteur Institute, Paris, France **The influence of cyproheptadine and of D-lysergamide on the rise in temperature induced by intracerebroventricular 5-hydroxytryptamine, noradrenaline and dopamine in conscious rabbits.** European Journal of Pharmacology (Amsterdam). 27(1):59-67, 1974.

Cyproheptadine and D-lysergamide (LSD), two known antagonists of the peripheral effects of serotonin (5-HT), were administered i.v. to conscious rabbits at different times before the intracerebroventricular (i.c.v.)administration of 5-HT, NAD or dopamine. Cyroheptadine (which had a slight hypothermic effect) antagonized the rise in temperature induced by 5-HT; this antagonism was dose related and appeared to be specific in that the hyperthermia induced by noradrenaline or dopamine was hardly modified. Interactions between LSD (which is hyperthermic alone) and 5-HT were more complex; both potentiation and depression were observed. 16 references. (Author abstract)

193452 Paalzow, Gudrun; Paalzow, Lennart; Stalby, Bjorn. Department of Pharmacology, Biomedical Center, University of Uppsala, Box 573, S-751 23 Uppsala, Sweden **Pentazocine analgesia and regional rat brain catecholamines.** European Journal of Pharmacology (Amsterdam). 27(1):78-88, 1974.

The analgesic activity of pentazocine was studied, utilizing an electrical method which makes it possible to study different pain reactions integrated at different levels within the central nervous system and the regional rat brain catecholamines and

their turnover were investigated as they relate to pentazocine analgesia. Inhibition of tyrosine hydroxylase, dopamine-beta-hydroxylase or pretreatment with L-dopa showed that an increased dopamine concentration and a decreased noradrenaline concentration antagonized the antinociceptive actions of pentazocine. After inhibition of tyrosine hydroxlase or dopamine-beta-hydroxylase, pentazocine accelerated the depletion of noradrenaline and dopamine. The most pronounced effect was found on dopamine in regions including the diencephalon - mesencephalon. It is suggested that the pentazocine induced increases of the threshold for vocalization and vocalization after discharge are related to a blockade of dopamine receptors and an increased turnover of noradrenaline. 46 references. (Author abstract modified)

193453 Hitzemann, Robert J.; Loh, Horace H. Langley Porter Neuropsychiatric Institute, University of California, San Francisco, CA 94143 **Further studies on the effect of p-hydroxynorephedrine (PONE) on norepinephrine metabolism in the rat brain.** European Journal of Pharmacology (Amsterdam). 27(1):89-98, 1974.

Rats pretreated i.c. with 10 micrograms of p-hydroxynorephedrine (PONE) were administered d-amphetamine and the effect of the combination of these drug treatments on behavior and the formation of 3H-norepinephrine (NE) from 3H-tyrosine was measured. PONE pretreatment blocked the d-amphetamine induced increase in exploratory activity but enhanced the production of d-amphetamine induced stereotyped behaviors. PONE pretreatment caused a 43% decrease in brain norepinephrine (NE) levels and this effect was potentiated by d-amphetamine. The in vivo formation of 3H-NE was decreased in animals administered d-amphetamine alone or PONE and d-amphetamine. However, these groups differed in the following respects: (a) d-amphetamine decreased the rate of disappearance of 3H-NE formed from 3H-tyrosine while PONE and d-amphetamine enhanced disappearance; (b) d-amphetamine decreased the formation of 3H-3-methoxy-4-hydroxyphenylglycol (MOPEG) while PONE and d-amphetamine enhanced 3H-MOPEG formation; (c) d-amphetamine enhanced 3H-NE release and decreased 3H-NE synthesis in a tissue slice preparation but PONE and d-amphetamine only enhanced 3H-NE release. The relevance of these findings to the effect of PONE pretreatment on d-amphetamine induced behavior is discussed. 38 references. (Author abstract)

193454 Gessner, Peter K. Department of Pharmacology, School of Medicine, State University of New York at Buffalo, Buffalo, NY **Failure of diphenylhydantoin to prevent alcohol withdrawal convulsions in mice.** European Journal of Pharmacology (Amsterdam). 27(1):120-129, 1974.

Alcohol withdrawal reactions were induced in mice using an established technique. Mice, administered 1.0mmole/kg pyrazole daily were exposed for 3 days to 10mg/l ethanol vapor and withdrawal was brought about by discontinuation of the exposure. Diphenylhydantoin (DPH) administered in doses of 12, 20 or 50mg/kg by either of two routes (i.p. or p.o.)failed to have any discernable effect on the withdrawal. A 100mg/kg dose of DPH increased seizure scores. Chloral hydrate administration in doses of 175, 244, or 350mg/kg, on the other hand, lowered seizure scores in a manner which was dose related and prompt. These findings suggest that the clinical use of DPH for control of the seizures seen in alcohol withdrawal should be reevaluated. The seizure scores of mice not exposed to ethanol but administered 1.0mmole/kg pyrazole daily for 3 days were negligible and well within values obtained with naive control mice not exposed to any pharmacological agent. 54 references. (Author abstract)

193455 Sangiah, Subbiah; Borowitz, Joseph L.; Yim, George K. W. Department of Pharmacology and Toxicology, Purdue University, Lafayette, IN 47907 **Actions of GABA, picrotoxin and bicuculline on adrenal medulla.** European Journal of Pharmacology (Amsterdam). 27(1):130-135, 1974.

The possibility that GABA, bicuculline and picrotoxin have important effects on the adrenal medulla was tested directly in isolated bovine adrenals; amino acids related to GABA were tested for comparison. It was found that GABA releases catecholamines from isolated perfused bovine adrenal glands, and that the secretory response is dependent on calcium and independent of acetylcholine. Tachyphylaxis to the releasing effect was also observed. It was found that picrotoxin inhibits the effect of acetylcholine and the effect of low but not high concentrations of GABA. Bicuculline, another reported GABA antagonist, was found to block the effect of all concentrations of GABA but not the effect of acetylcholine. Bicuculline is therefore a more specific GABA blocker in adrenal medulla than picrotoxin. These findings suggest the existence of GABA receptors in adrenal medulla which may be analogous in some respects to those reported in autonomic ganglia. 19 references. (Author abstract modified)

193456 Fauley, Jon J.; Fuller, Dennis R.; LaPidus, Jules B. Chemical Abstracts, 4290 Olentangy River Rd., Columbus, OH 43210 **The stereoselective inhibition of lipolysis by nonphenolic phenethylamines.** European Journal of Pharmacology (Amsterdam). 27(1):136-140, 1974.

Inhibition of norepinephrine induced lipolysis by the stereoisomers of ephedrine and phenyl-2-piperidyl carbinol and the diastereomers of 8-hydroxy-6,7-benzomorphan was investigated in rat adipose tissue, in vitro. Relative inhibitory actions of stereoisomers were observed. In each series, the erythro configuration was best accommodated by the adrenergic adipose tissue receptor system. 12 references. (Author abstract modified)

193457 Vasko, Michael R.; Domino, Laurence E.; Domino, Edward F. Department of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Differential effects of d-amphetamine on brain acetylcholine in young, adult, and geriatric rats.** European Journal of Pharmacology (Amsterdam). 27(1):145-147, 1974.

To establish the effects of d-amphetamine on rats as function of their age, varying doses of d-amphetamine were given i.p. to young (28-day-old), adult (approximately 90-day-old), and geriatric rats (approximately 2 years old). Thirty minutes after injection, rats were sacrificed and acetylcholine (Ach) extracted and assayed by pyrolysis gas - liquid chromatography. Total brain Ach levels were not significantly different among the control animals in all three groups. d-Amphetamine however, decreases total levels of Ach in young and geriatric rats without changing levels in adult animals. The changes in young rats were dose related; these results suggest an important difference in brain cholinergic mechanisms depending upon age. 12 references. (Author abstract)

193458 Koyuncuoglu, H.; Gungor, M.; Sagduyu, H.; Eroglu, L. Department of Pharmacology, Medical School of Istanbul Univ., Istanbul, Turkey **The antagonistic effects of aspartic acid on some effects of morphine on rats.** European Journal of Pharmacology (Amsterdam). 17(1):148-150, 1974.

The decrease in spontaneous motor activity and the increase in analgesic threshold by morphine in rats were antagonized by aspartic acid. The lethal dose of morphine in rats was increased more than two fold by aspartic acid. 12 references. (Author abstract)

193541 Engstrom, Gunnar; Svensson, Torgny H.; Waldeck, Bertil. Department of Anatomy, University of Goteborg, Goteborg, Sweden **Thyroxine and brain catecholamines: increased transmitter synthesis and increased receptor sensitivity.** Brain Research (Amsterdam). 77(3):471-483, 1974.

In a study of the effects of thyroxine on brain catecholamines (CA), mice were given eight subcutaneous injections of L-thyroxine sodium (T4) at 12 h intervals. One hour after the last injection the brain concentration of noradrenaline (NA), but not of dopamine (DA), was significantly reduced. The accumulation of DOPA in the brain during 30 min after treatment with an aromatic amino acid decarboxylase inhibitor was significantly enhanced 5 and 15 h after the last T4 injection, indicating increased synthesis of (CA). Twelve hours after the last T4 administration, the brain accumulation of homovanillic acid following treatment with probenecid was twice the control value. The plasma level of thyroxine was increased, when measured 2-12h after the last thyroxine injection, but no correlation was found between the plasma level and the rate of CA synthesis in the brain. The T4 regimen caused significant cardiomegaly. Six hours after the last T4 injection, the exploratory or the spontaneous locomotor activity of mice was not affected. The data imply increased turnover of brain CA following pretreatment with thyroxine, as well as increased sensitivity of brain CA receptors. 37 references. (Author abstract modified)

193544 Marsden, C. D.; Dolphin, A.; Duvoisin, R. C.; Jenner, P.; Tarsy, D. University Department of Neurology, Institute of Psychiatry, Denmark Hill, London SE5, England **Role of noradrenaline in levodopa reversal of reserpine akinesia.** Brain Research (Amsterdam). 77(3):521-525, 1974.

The possibility that the reversal by levodopa of the akinetic rigid syndrome produced by reserpine depends upon changes in noradrenaline as well as dopamine levels was investigated in mice. Results suggest that: noradrenaline formed from levodopa may play a role in causing reversal of reserpine akinesia; the levodopa reversal may require the formation of noradrenaline as well as dopamine; and the efficacy of levodopa in Parkinsonism may be due not only to the formation of dopamine but also noradrenaline. 21 references.

193547 Ebadi, Manuchair S.; Simmons, Vickie J.; Hendrickson, Merrill J.; Lacy, Priti S. Department of Pharmacology, University of Nebraska College of Medicine, Omaha, NB 68105 **Pharmacokinetics of lithium and its regional distribution in rat brain.** European Journal of Pharmacology (Amsterdam). 27(3):324-329, 1974.

Transportation and distribution of lithium salts in the brain tissues of adult rats were studied. Sixteen areas of the animals' brains were assessed for specific activity of lithium and pharmacokinetics and regional distribution of other solutions are reported. The experimental evidence indicates that lithium is distributed unevenly in the brain. Among areas studied, the highest concentrations of lithium were found in the basal ganglia and the pituitary, and the lowest in the spinal cord, pons, and medulla. Lithium distributions in 12 other body organs were also analyzed. Absorbance, time, and dosages for the various areas of the brain are included. 25 references. (Author abstract modified)

193550 Nistri, Andrea; Pepeu, Giancarlo. Dept. of Pharmacology, St. Bartholomew's Hospital Medical College, University of London, Chearterhouse Square, London E.C. 1M 6BQ, England **Acetylcholine levels in the frog spinal cord following the administration of different convulsants.** European Journal of Pharmacology (Amsterdam). 27(3):281-287, 1974.

The effects of strychnine, brucine, thebaine, bicuculline, picrotoxin, and leptazol on the acetycholine (ACh) levels in the frog spinal cord were investigated at different times of the year. Strychnine and thebaine caused an increase in the spinal ACh content when the seizures lasted from 3 to 4 hours. Bicuculline and picrotoxin only caused a decrease in the ACh concentration, 10-15 min after injection. Leptazol initially increased the level of ACh, but following prolonged seizures, the ACh concentration was not affected. The experiments show that each type of convulsant affected ACh stores in a different way. 34 references. (Author abstract modified)

193577 Lal, S.; Papeschi, R.; Duncan, R. J. S.; Sourkes, T. L. Department of Psychiatry, McGill University, Montreal, Quebec, Canada **Effect of copper loading on various tissue enzymes and brain monoamines in the rat.** Toxicology and Applied Pharmacology. 28(3):395-405, 1974.

The possible effect of copper loading on dopa decarboxylase (DDC), monoamine oxidase (MAO), other tissue enzymes and on the liver was investigated, in rats. Three-week-old rats were injected daily for 2, 4, or 6 weeks. Controls received physiological saline. Copper treated animals showed an increased mortality and a decrease in body weight. After 6 weeks of copper loading, renal copper concentration increased 14 fold but there was no effect on lactate dehydrogenase, succinate dehydrogenase, malate dehydrogenese, DDC or MAO. Brain copper increased after 6 weeks of copper administration. The adrenal glands of copper treated rats were markedly increased. The results indicate that copper loading can affect enzymes involved in monoamine metabolism and other thiol containing enzymes at very high hepatic copper concentrations. The relative protection of liver enzymes and the absence of any effect of copper on renal enzymes may be related to intracellular distribution. 68 references. (Author abstract modified)

193588 Donaldson, John. McGill University **Regional distribution of cations and their relation to the neurochemistry of experimental epilepsy, neurotransmitters and ATP'ase in the central nervous system. (Ph.D. dissertation).** Dissertation Abstracts International. Ottawa, National Library of Canada.

Na+, K+, Ca2+, Mg2+, Cu2+, Zn2+, and Mn2+ were determined in several regions of rat brain using atomic absorption spectroscopy. Copper was highest in the hypothalamus and lowest in the medulla oblongata. Zinc was also low in the medulla oblongata and highest in the hippocampal region. Manganese was found in high concentration in the hypothalamus. Administration of Cu2+ and Zn2+, or of the cardiac glycoside, ouabain, by intraventricular injection in cannulated rats resulted in epileptic seizures and was correlated with the ability of these agents to inhibit brain Na+-K+-ATP'ase both under in vitro and in vivo conditions. Administration of L-DOPA, reserpine and a pheonthiazine derivative chronically to rats resulted in alteration of the endogenous mental content in specific brain regions. Injection of the monovalent ions, lithium and rubidium, resulted in alteration of mouse brain biogenic amine content. (Journal abstract modified)

193777 Rinaldi, Patricia C. University of Denver **The effects of drugs regulating autonomic responses during conditioning on subsequent avoidance behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-30190 HC$12.50 MF$4.00 98 p.

The effect of drug regulation of autonomic responses during pretraining on subsequent avoidance conditioning involving the same conditioned stimulus (CS) was studied in 60 rats. Adrenaline or noradrenaline was injected to produce sympathetic arousal during pretraining; tetraethyl ammonium was injected to produce autonomic blockage. Classical conditioning pretraining for three drug groups and one saline group consisted of eight trials pairing 70 lb, 600 HZ +one (CS) and a .1-.15 ma tail shock (UCS). A fifth group received saline and unpaired tone and shock presentations, while a sixth received no pretraining or drug. Both habituating response (HR) and behavior measures were recorded, with HR indicating effectiveness of the drug used, responsivitiy to CS and UCS, adaptation, and conditioning. Drug regulation of autonomic responses during pretraining had no significant effect on subsequent avoidance. Emotionality as inferred from freezing to the CS was involved in mediating performance outcomes in avoidance conditioning. Findings are discussed in relation to theories of autonomic nervous system regulation and emotion. (Journal abstract modified)

193797 Celesia, Gastone G.; Chen, Rong-Chi. Department of Neurology, Neurological and Rehabilitation Hospital, 1954 East Washington Ave., Madison, WI 53704 **Effects of Ketamine on EEG activity in cats and monkeys.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 37(4):345-353, 1974.

The effect of Ketamine on the cortex of normal and epileptic animals was assessed in 28 cats and six monkeys, using EEG data. In cats, Ketamine initially induced generalized high voltage beta activity followed by generalized slow waves. These slow waves were called Ketamine complexes (KCs) and had two different morphological appearances suggestive either of polyspike slow wave complexes or of delta waves intermixed with beta activity. In monkeys, Ketamine induced theta and beta rhythms and at higher doses, quasi periodic slow wave complexes. Ketamine consistently suppressed focal seizures but was ineffective in modifying interictal epileptogenic activity both at the primary and mirror focus. It is concluded that Ketamine has no epileptogenic properties. Ketamine affects the central nervous system at many levels in different ways. It simultaneously excites and depresses different systems and disrupts normal cortical and subcortical physiological activities. 13 references. (Author abstract modified)

193803 Spencer, Hugh J.; Havlicek, Viktor. Department of Physiology, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba R3E OW3, Canada **Alterations by anesthetic agents of the responses of rat striatal neurons to iontophoretically applied amphetamine, acetylcholine, noradrenaline, and dopamine.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(4):808-813, 1974.

The effects of two anesthetic agents, Penthrane (methoxyflurane) and diallylbarbiturate (Dial), were investigated on the responses of rat striatal neurons to iontophoretically applied noradrenaline (NA), dopamine (DA), acetylcholine (ACh), and d-amphetamine (d-Amph). At both high (50mg/kg) and low (35mg/kg) dose levels of diallylbarbiturate there was a highly significant change in the nature of the responses to all the substances tested. This change was primarily a decrease in the frequency of excitatory responses observed to catecholamine and ACh, compared with those observed under Penthrane. Although the dosage of diallylbarbiturate also affected the nature of the responses, it was to a much lesser degree; d-Amph responses were not affected and were almost purely inhibitory. Under both anesthetics, there was no evident correlation between the responses to d-amphetamine and to catecholamines. 20 references. (Author abstract modified)

194153 Datta, R. K.; Antopol, W.; Ghosh, J. J. Division of Laboratories, Beth Israel Medical Center, New York, NY 10003 **Mescaline-induced changes of brain-cortex ribosomes: effect of mescaline on ribosomal synthesis of polyuridine-directed polyphenylalanine.** Naunyn Schmiedebergs Archives of Pharmacology (Berlin). 277(3):319-322, 1973.

Mescaline induced changes of goat brain cortex ribosomes were investigated. It was found that pretreatment of brain cortex slices with mescaline causes decreased synthesis of polyphenylalanine by ribosomes isolated from drug treated slices under the direction of messenger polyuridine not exposed to mescaline. 7 references. (Author abstract modified)

194155 Tomosky, Thomas Keith; Bennett, James L.; Bueding, Ernest. Dept. of Pathobiology, School of Medicine, Johns Hopkins University, Baltimore, MD **Tryptaminergic and dopaminergic responses of Schistosoma mansoni.** Journal of Pharmacology and Experimental Therapeutics. 190(2):260-271, 1974.

Pharmacological evidence is reported indicating that 5-hydroxytryptamine (5-HT) is an excitatory neurotransmitter in the worm Schistosoma mansoni and that Schistosoma mansoni may be useful in assaying compounds for potential dopamine (DA) agonist or antagonist activity. The stimulation of the motor activity of adult schistosomes brought about by cholinergic blockade is abolished by bromlysergic acid diethylamide and other 5-HT antagonists and by prior 5-HT depletion brought about by exposure of the parasites to chlorimipramine and reserpine. Whereas catecholamines have no effect on the motor activity of schistosomes, low concentrations of DA, norepinephrine (NE), and epinephrine (but not isoproterenol) produce a lengthening response of the worm which is ascribed to a relaxation of the longitudinal musculature. The same response was induced by apomorphine, considered to be a specific DA receptor agonist, but not by clonidine, a specific NE receptor agonist. Apomorphine and DA were more potent in this respect than NE and epinephrine. These effects are blocked more effectively by DA blocking agents than by alpha-adrenergic and beta-adrenergic blockers. 38 references. (Author abstract modified)

194156 Shad, Nandkumar S.; Patel, S. R.; Gulati, O. D. Ensor Research Labs., William S. Hall Psychiatric Institute, P. O. Box 119, Columbia, SC 29202 **Potentiation by 3,4-dimethoxyphenylethylamine (DMPEA) and cocaine of norepinephrine-induced contraction of guinea-pig vas deferens.** Journal of Pharmacology and Experimental Therapeutics. 190(2):227-233, 1974.

The influence of 3,4-dimethoxyphenylethylamine (DMPEA) and of cocaine on the responses of isolated guinea-pig vas deferens to norepinephrine (NE), methoxamine, acetylcholine (ACh) and histamine was examined. Alone DMPEA and cocaine did not exert any effect on the vas deferens but shifted the dose response curves for the contractile effect of NE to the left and also increased the maximal responses. The contractile responses to NE were potentiated by lower concen-

trations of cocaine than of DMPEA. Cocaine and DMPEA were equally effective in producing a leftward shift of the dose response curve for the contractile effect of methoxamine. Both DMPEA and cocaine produced slight shifts of the ACh and histamine dose response curves; the maximum responses to ACh were significantly increased whereas those to histamine were not affected. Denervation induced a greater shift of the NE dose response curve than that induced by cocaine. Cocaine induced supersensitivity has both prejunctional and postjunctional components, is specific for NE, and is due to interference with the neuronal uptake process; DMPEA induced supersensitivity is almost entirely postjunctional. 23 references. (Author abstract modified)

194169 Devi, S. Parvathi; Rao, A. Venkoba; Hariharasubramanian, N.; Srinivasan, V. Dept. of Physiology, Madural Medical College, Madurai, India **Lithium and adrenal cortex.** Indian Journal of Psychiatry (Madurai). 15(3):250-256, 1973.

Lithium - adrenocortical interlinks were observed in healthy rats. The adrenocortical cytological changes, the absolute eosinophil values as indexes on adrenocortical oxycorticoid secretion, and pineal cytological changes as possibly indicative of fluctuations in aldosterone secretion were studied. The findings indicated distinct adrenocortical responses to lithium. It is suggested that lithium displaces intracellular sodium, particularly in the central nervous system; thus, lithium could dampen neural transmissions. Under conditions of excessive intracellular sodium accumulation, such as occurs in affective disorders, the attenuating effects of lithium upon neural transmissions may result in signs and symptoms of improvement. Observations of pineal cytological changes in rats treated with lithium are fully discussed. 15 references. (Author abstract modified)

194541 Suria, Amin; Lehne, Richard; Costa, E. Lab. of Prelinical Pharmacology, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Possible mechanism of action of benzodiazepines. (Unpublished paper).** Washington, D.C., NIMH, 1974. 21 p.

The effects of diazepam on the synaptic potentials in the sympathetic ganglia were investigated. Posttetanic potentiation (PTP) of slow inhibitory postsynaptic potential (s-IPSP) in curarized sympathetic bullfrog ganglia was recorded by the sucrose gap technique. Diazepam potentiated the PTP of s-IPSP in a dose dependent fashion. Findings suggest that cyclic 3',5'-adenosine monophosphate (cAMP) may contribute to the action of diazepam. It is postulated that diazepam facilitates the increase of cAMP levels possibly by inhibiting the cAMP phosphodiesterase activity. The elevated levels of cAMP, in turn, may contribute to the increased hyperpolarization seen in the presence of diazepam, thus facilitating the PTP of s-IPSP. If anxiety is related to the increased firing rate of neurons, diazepam may exert its antianxiety activity by facilitating the hyperpolarization, thus making the neurons quiescent. 19 references. (Author abstract modified)

194571 Quadri, Syed Kaleemullah. Michigan State University **Effects of central acting drugs and ergot derivatives on prolactin and growth hormone secretion, on growth of pituitary and mammary tumors and on reproduction in old rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-13956 HC$12.50 MF$4.00 406 p.

The effects of central acting drugs and ergot derivatives on prolactin and growth hormone secretion, on growth of pituitary and mammary tumors and on reproduction in old rats were investigated. Daily treatment of rats carrying pituitary tumor transplants with ergocornine produced regression of tumor growth, degeneration of tumor tissue and suppression of prolactin but not growth hormone (GH) secretion. Ergocornine and ergocryptine produced marked regression of spontaneous mammary tumors in old female rats. It was concluded that the ergot derivatives inhibited mammary tumor growth by depressing prolactin secretion. The ergot derivatives, ergocornine and lysergic acid diethylamide (LSD) also inhibited growth of carcinogen induced mammary tumors. High doses of androgens, like high doses of estrogens, may inhibit mammary tumor growth by interfering with the peripheral action of prolactin on tumor parenchyma. Evidence was obtained that mammary tumor growth can be altered by altering catecholamine activity in the hypothalamus. (Journal abstract modified)

194700 Kumar, Amresh. University of Illinois at Urbana-Champaign **Physiologic, biochemical, and clinical effects of ketamine hydrochloride in goats (Capra hircus) with and without premedication. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-5616 HC$12.50 MF$4.00 250 p.

The physiologic, biochemical, and clinical effects of ketamine hydrochloride were investigated in goats with and without premedication. Administration of ketamine with and without atropine, acetylpromazine, or diazepam caused a significant increase in respiratory rate, heartrate, and mean arterial blood pressure at maximal depth of anesthesia. The administration of atropine + xylazine + ketamine was followed by a significant rise in blood glucose at maximal depth of anesthesia. Administration of xylazine caused a significant decrease and atropine an increase in heartrate. Intramuscular administration of ketamine at the rate of 10mg/lb to 6 pregnant goats near term caused an increase in heartrate, mean arterial blood pressure, PcCo2, and a decrease in pH and PaO2 in the mother and fetus 5 minutes after its administration. Supplemental drug increments required to prolong surgical anesthetic period were either with ketamine alone or a mixture of xylazine and ketamine, permitting surgical anesthesia for 2.25-2.75 hours. (Journal abstract modified)

194742 Krieglstein, J.; Stock, R. Pharmakologisches Institut der Universitat, D-6500 Mainz, Obere Zahlbacher Str. 67, Federal Republic of Germany **Comparative study of the effects of chloral hydrate and trichloroethanol on cerebral metabolism.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 277(4):323-332, 1973.

The isolated perfused rat brain was used for a comparative study of the effects of chloral hydrate and trichloroethanol on cerebral energy metabolism. Little more than 10% of chloral hydrate in the isolated brain and in the perfusion medium were reduced to trichloroethanol. In intact animals there was about 70% of chloral hydrate transformed. Chloral hydrate and trichloroethanol caused an accumulation of P-creatine, no change in the lactate/pyruvate ratio, an increase of the glucose concentration and a decrease of glucose-6-P level in the isoalted brain. The rise of brain glucose level was more pronounced after trichloroethanol than after chloral hydrate. The effects of chloral hydrate and trichloroethanol on brain glucose and glucose-6-P levels suggest an inhibition of brain hexokinase activity by these drugs. 21 references. (Author abstract modified)

194743 Gruner, J.; Krieglstein, J.; Rieger, H. Pharmakologisches Institut der Universitat Mainz, D-6500 Mainz,

Obere Zahlbacher Str. 67, Federal Republic of Germany **Comparison of the effects of chloral hydrate and trichloroethanol on the EEG of the isolated perfused rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 277(4):333-348, 1973.

An isolated perfused rat brain preparation was used to compare the effects of chloral hydrate and its metabolite trichloroethanol on the EEG. Both drugs exhibited CNS depressant activity. The changes in the EEG caused by trichloroethanol seemed to be completed after 5 minutes of perfusion, whereas EEGs from the chloral hydrate perfusions gradually changed, becoming similar to the EEGs from trichloroethanol perfusions after 15 minutes. Trichloroethanol is more active than chloral hydrate even if only during the first 10 minutes of perfusion greater effects of trichloroethanol on the EEG were detectable. 23 references. (Author abstract modified)

194744 Ahtee, Liisa; Kaariainen, I. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **5-Hydroxytryptamine in platelets and brain of rabbits treated chronically with imipramine, morphine or methadone.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 277(4):429-436, 1973.

The effects of chronic administration of methadone were compared with the effects of imipramine on platelet 5-hydroxytryptamine (5-HT). Results suggest that methadone in high enough doses which can be given only to tolerant animals inhibits the uptake of 5-HT into platelets in vivo. The different effects of chronic administration of imipramine and methadone on brain 5-HT indicate that in addition to inhibiting uptake these drugs may have effects also on other processes regulating the 5-HT content of the brain. 16 references. (Autho abstract modified)

194925 Askew, W. E.; Ho, B. T. Department of Psychiatry, Baylor College of Medicine, Houston, TX 77025 **Effects of tetrahydrocannabinols on cyclic AMP levels in rat brain areas.** Experientia (Basel). 30(8):879-880, 1974.

The effects of tetrahydrocannabinols on the concentration of rat brain cyclic AMP is described. While delta9-THC exerted no significant changes in cyclic AMP levels in the rat brain areas examined, its isomer, delta8-THC, produced a significant increase of cyclic AMP content in the midbrain and slight decreases of the cyclic nucleotide in the cerebellum and medulla. The elevation of cyclic AMP in the midbrain by delta8-THC could be the result of a decreased turnover of the cyclic nucleotide. 14 references.

194927 Henkin, R. I.; Stillman, I. S.; Gilbert, D. L.; Lipicky, R. J. Section on Neuroendocrinology, NHLI, NIH, Building 10, Room 7D16, Bethesda, MD 20014 **Ineffectiveness of lysergic acid diethyl amide-25 (LSD) on altering Na-K currents in squid giant axon.** Experientia (Basel). 30(8):916-917, 1974.

The effects of lysergic acid diethyl amide on the basic events which produced the neuraxon potential in squid giant axon were investigated. Single neuronal units in the midbrain raphe nuclei of rat exhibit significant inhibition of spontaneous firing rate after parenteral administration of minute amounts of LSD. Results demonstrate that administration of massive concentrations of LSD do not alter the basic ionic events which give rise to the action potential. LSD-25 seemed effective in altering some aspects of neural activity in the squid but it is ineffective in altering the basic ionic events. LSD does affect synaptic conduction, one effect being its blocking action of serotonergic postsynaptic receptor sites. 19 references.

194928 Krieglstein, J.; Meffert, A.; Niemeyer, D. H. Institut fur Pharmakologie und Toxikologie im FB/6 der Philipps Universitat Marburg, Deutschhausstrasse 17, D-355 Marburg, Germany **Influence of emulsified fat on chlorpromazine availability in rabbit blood.** Experientia (Basel). 30(8):924-926, 1974.

The influence of a commercially available fat emulsion on the fraction of free chlorpromazine (CPZ) in rabbit blood, as well as its influence on the acute toxicity of CPZ in rabbits, was investigated. In comparison with normal blood, there was no significant change of free CPZ concentration by the xylitol solution added. A fat emulsion in blood appears able to take up lipophilic drugs, reduce their fraction dissolved in plasma water and thus decrease their actual availability at the sites of action. 14 references.

194929 Beaton, J. M.; Pegram, G. V.; Smythies, J. R.; Bradley, R. J. Neurosciences Program and Department of Psychiatry, University of Alabama Medical Center, University Station, Birmingham, AL 35294 **The effects of nicotinamide on mouse sleep.** Experientia (Basel). 30(8):926-927, 1974.

The effects of nicotinamide on mouse sleep were studied on 30 adult, male mice. High doses of nicotinamide may have behavioral effects unconnected with its role as a vitamin. The best known drug that increases REM is reserpine. This suggests that a further pharmacological study of nicotinamide in this light might be of interest. 13 references.

194930 Little, H. J.; Rees, J. M. H. Department of Pharmacology, Materia Medica and Therapeutics, University of Manchester, Manchester, M13 9PT, England **Tolerance development to the antinociceptive actions of morphine, amphetamine, physostigmine and 2-aminoindane in the mouse.** Experientia (Basel). 30(8):930-932, 1974.

The development of tolerance to the antinociceptive action of morphine was described. The possibility of cross-tolerance between it, morphine, amphetamine, and physostigmine was explored. Tolerance developed to the actions of all four drugs. The existence of cross-tolerance between morphine and amphetamine is compatible with the previous observation of cross-tolerance between morphine and methylamphetamine. Cross-tolerance between either drug and the stereochemically more rigid sympathomimetic 2-aminoindane is reported. 24 references.

195042 Thomsen, Klaus; Olesen, O. Vendelin. Psychopharmacology Research Unit, Statshospitalet, DK-8240 Risskov, Denmark **Long-term lithium administration to rats. Lithium and sodium dosage and administration, avoidance of intoxication, polyuric control rats.** International Pharmacopsychiatry (Basel). 9(2):118-124, 1974.

Long-term lithium administration to rats was examined. The lithium treated rats drank more saline than controls. The extra sodium intake resulted in a 50% higher total fluid intake by the lithium treated rats than by the controls. Equally large fluid intakes of the two groups were obtained by adding more sodium to the food of the control animals and less to the food of the lithium treated rats. During the following 2 months, the mean serum lithium concentration was 1.1mM and no signs of intoxication occurred. The administration of extra sodium to the lithium treated rats did not abolish the lithium induced lowered antidiuretic response to vasopressin. By appropriate adminstration of the lithium and sodium intakes it was possible to maintain rats at a serum lithium level 0.7-1mM for long periods of time without signs of intoxication and with the same bodyweight as control rats. 2 references. (Author abstract modified)

195046 Sethy, V. H.; Van Woert, M. H. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Brain acetylcholine and cholinesterase: effect of phenothiazines and physostigmine interaction in rats.** Journal of Neurochemistry (Oxford). 23(1):105-109, 1974.

The effect of phenothiazines either alone or in combination with physostigmine on whole brain acetylcholine concn and cholinesterase activity has been investigated in male rats. Phenothiazines (cholpromazine, trifluperazine and thioridazine) when injected alone had no significant effect on brain acetylcholine concentration. Pretreatment with chlorpromazine and thioridazine significantly enhanced the physostigmine induced increase in brain acetylcholine concn and inhibition of cholinesterase activity. Trifluperazine had no significant effect on the physostigmine induced increase in brain acetylcholine concentration and inhibition of cholinesterase activity. The potentiation of the physostigmine induced increase in brain acetylcholine concn by phenothiazines may be due to increased acetylcholine turnover secondary to the blockade of dopamine receptors by neuroleptic drugs and decreased acetylcholine catabolism because of enhanced cholinesterase inhibition. 28 references. (Author abstract)

195048 Nicklas, W. J.; Berl, S.; Clarke, D. D. Department of Neurology, Mt. Sinai School of Medicine, CUNY, Fifth Avenue and 100th St., New York, NY 10029 **Interaction of catecholamine and amino acid metabolism in brain: effect of pargyline and L-dopa.** Journal of Neurochemistry (Oxford). 23(1):149-157, 1974.

The effect of pargyline and L-dopa on the interaction of catecholamine and amino acid metabolism in rat brain were examined. The combination of L-DOPA and pargyline caused a decrease in level of aspartate and an increase in that of glutamine in vivo in cerebral cortex, cerebellum, brain stem, hypothalamus, neostriatum and cervical cord of rat. Pargyline alone caused a stimulation of the labeling of glutamate and aspartate but not glutamine and GABA; the levels of aspartate and GABA were greater than in control slices. The addition of L-DOPA to slices from pargylinized animals caused a severe decrease in glutamine labeling but not in that of glutamate or aspartate; the level of glutamine was increased while that of glutamate was decreased. The results are discussed in terms of the known biochemical and morphological compartmentation of amino acids in brain. It is suggested that catecholamines, in the process of functioning as transmitters, may also function as metabolic regulators of other transmitters, e.g. amino acids, as well as of the energy required for balanced neuronal function. 22 references. (Author abstract modified)

195049 Chiueh, C. C.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **In vivo release of endogenously synthesized catecholamines from the cat brain evoked by electrical stimulation and by d-amphetamine.** Journal of Neurochemistry (Oxford). 23(1):159-168, 1974.

The in vivo release of endogenously synthesized catecholamines from the cat brain evoked by electrical stimulation and by d-amphetamine was reported. The cerebral ventricles of spinal sectioned cats were perfused with artificial cerebrospinal fluid after the intraventricular administration of (3H)DOPA or (3H)tyrosine. Endogenously synthesized (3H)dopamine or (3H)norepinephrine were identified in the perfusate. Electrical stimulation of catecholaminergic nerve tracts in the hypothalamus increased the efflux of both catecholamines. The addition of d-amphetamine to the perfusing cerebrospinal fluid caused a large increase in (3H)dopamine and a small increase in (3H)norepinephrine appearing in the perfusate. Most of the endogenously synthesized (3H)catecholamines detected in the perfusate following stimuli originated from structures bordering the lateral cerebral ventricle. Norepinephrine and dopamine were synthesized in and released for catecholaminergic nerve terminals in structures bordering the cerebral ventricles. 42 references. (Author abstract)

195054 Corbett, L.; Christian, S. T.; Monti, J. A.; McClain, L. D. Neurosciences Program, University of Alabama in Birmingham, Birmingham, AL 35294 **Inhibition of synaptic vesicular Mg+2 dependent ATPase ('stenin') by antipsychotic phenothiazines.** Research Communications in Chemical Pathology and Pharmacology. 8(4):607-614, 1974.

A series of antipsychotic phenothiazines were found to be potent inhibitors of the Mg+2 dependent ATPase associated with synaptic vesicles isolated from rat brains. Findings suggest that these compounds act therapeutically at the synaptic level. The implications of these data for the pathophysiology of phenothiazine responsive psychoses are discussed. 13 references. (Author abstract)

195091 Cicero, T. J.; Meyer, E. R.; Bell, R. D. Department of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Effects of phenoxybenzamine on the narcotic withdrawal syndrome in the rat.** Neuropharmacology (Oxford). 13(7):601-607, 1974.

The effects of various alpha-adrenergic and beta-adrenergic blocking agents on the narcotic withdrawal syndrome in rats were determined. Alpha-adrenergic blockers caused a dose dependent suppression of two behavioral responses characteristic of precipitated narcotic withdrawal in the rat: diarrhea and, most notably, wet dog shakes. The beta-adrenergic blocker, propranolol, did not effect the expression of the narcotic withdrawal syndrome. The effects of alpha-blockers on withdrawal behavior did not appear to be due to the slight degree of sedation produced by the highest doses of the drugs, because pentobarbital and promethazine, in doses sufficient to induce marked sedation and anesthesia, did not decrease the severity of withdrawal. In fact, pentobarbital appeared to exacerbate the abstinence syndrome. 18 references. (Author abstract)

195093 Diaz, P. M. Department of Anesthesiology, University of Miami School of Medicine, P.O. Box 875, Biscayne Annex, Miami, FL 33152 **Interaction of pentylenetetrazol and trimethadione on the metabolism of serotonin in brain and its relation to the anticonvulsant action of trimethadione.** Neuropharmacology (Oxford). 13(7):615-621, 1974.

The interaction between the anticonvulsant trimethadione and the convulsant metrazol on the metabolism of brain serotonin was studied in rats. Trimethadione alone produced a 28-44% increase in the rate of synthesis of brain serotonin. The same dose of trimethadione plus 30 or 50mg/kg of metrazol produced no change in the rate of synthesis of brain serotonin and no seizures. Trimethadione plus 75mg/kg of metrazol produced a 55% decrease in the rate of synthesis of brain serotonin and a marked increase in locomotor activity, but no clonic - tonic seizures. Reserpine produced a 62% decrease in the mean convulsive dose of metrazol in rats treated with trimethadione. p-Chlorophenylalanine produced a 26% decrease in mean convulsive dose, which was reversed by 5-hydroxytryptophan. Alpha-methyltyrosine and 5-hydroxytryptophan had no effect on mean convulsive dose. 14 references. (Author abstract modified)

195094 Glisson, S. N.; Karczmar, A. G.; Barnes, L. Department of Pharmacology and Therapeutics, Loyola University Stritch School of Medicine, Maywood, IL 60153 **Effects of diisopropyl phosphofluoridate on acetylcholine, cholinesterase and catecholamines of several parts of rabbit brain.** Neuropharmacology (Oxford). 13(7):623-631, 1974.

Diisopropyl phosphorofluoridate (DFP) was administered to rabbits in which the pretreatment with a monoamine oxidase inhibitor, JB835, and DOPA caused an elevation in norepinephrine (NE) and, to a lesser extent, in dopamine (DA) levels in the thalamus, hypothalamus, midbrain and hippocampus. Pretreatment with JB835 - DOPA combination and/or elevation of NE and of DA caused no significant effect upon either cholinesterase activity or acetylcholine (ACh) levels in the caudate nucleus, midbrain, thalamus or hypothalamus. Diisopropyl phosphorofluoridate caused nearly complete inhibition of cholinesterase activity in all these brain parts whether or not the animals were pretreated with JB835 and DOPA, and with atropine. Diisopropyl phosphorofluoridate caused a decrease of NE levels and elevation of DA levels in all four brain parts of the pretreated rabbits. Dopamine was affected maximally in the hypothalamus, midbrain and thalamus concomitantly with major increments in ACh at these sites. Maximal decreases in NE occurred in the caudate, thalamus and midbrain; the extent of these changes did not parallel that of the changes in ACh. 38 references. (Author abstract modified)

195095 Sinclair, J. G.; Sastry, B. S. R. Division of Pharmacology and Toxicology, University of British Columbia, Vancouver, British Columbia, Canada V6N 1W5 **The blockade of bulbospinal inhibition by imipramine, desipramine and pargyline.** Neuropharmacology (Oxford). 13(7):643-650, 1974.

Bulbospinal inhibition of the spinal cord monosynaptic reflex antagonized by imipramine HCl, desipramine HCl and pargyline HCl in unanesthetized, decerebrate cats was reported. The blocking action of imipramine was prevented in aminals pretreated for three consecutive days with DL-p-chlorophenylalanine (300mg/kg) but not in animals pretreated with DL-alpha-methyl-p-tyrosine methyl ester HCl (125mg/kg) 16 and 4 hr prior to recording. These results do not support the proposal that the bulbospinal inhibitory pathway contains a 5-hydroxytryptamine (5-HT) link. The findings suggest that 5-HT is involved in antagonizing bulbospinal inhibition of the monosynaptic reflex. 27 references. (Author abstract modified)

195096 Palmer, G. C.; Manian, A. A. Department of Pharmacology, University of New Mexico School of Medicine, Albuquerque, NM 87131 **Inhibition of the catalytic site of adenylate cyclase in the central nervous system by phenothiazine derivatives.** Neuropharmacology (Oxford). 13(7):651-664, 1974.

Inhibition by phenothiazine derivatives was evaluated with respect to the catalytic component of adenylate cyclase prepared from either a high speed particulate fraction of rat cerebral cortex and hypothalamus or neuronal and glial enriched fractions from rat and rabbit cerebral cortex. The dihydroxylated analogs of chlorpromazine, prochlorperazine, perphenazine and promazine along with the dioxo form of chlorpromazine were the most potent inhibitors of either basal activity or fluoride activation of the enzyme. To a lesser extent inhibition of adenylate cyclase was observed with the parent compounds (including fluphenazine and promethazine) and their respective monohydroxylated or methoxylated analogues. The enzyme from the high speed particulate fraction was more resistant to inhibition by these compounds than the neuronal and glial enzymes. The data suggest that the actions of specific metabolites of phenothiazines may account for additional intracellular effects following experimental or therapeutic administration of any parent compound. 45 references. (Author abstract modified)

195097 Sherman, A.; Gebheart, G. F. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Regional levels of GABA and glutamate in mouse brain following exposure to pain.** Neuropharmacology (Oxford). 13(7):673-675, 1974.

A study of the effects of pain on regional brain levels of gamma amino butyric acid (GABA) and glutamate were performed using male CFI mice. Gas chromatographic analysis revealed no significant differences in these substrates in subcortical areas. In the cortical areas, pain produced a significant elevation of GABA levels and a small, but significant, decrease in glutamate levels. Neither of these changes was observed in animals pretreated with morphine before exposure to pain. Restraint stress failed to produce the same changes. The ratio of GABA to glutamate was a reliable index of exposure to pain. 7 references. (Author abstract)

195112 Jakubovic, A.; McGeer, P. L. Kinsmen Laboratory of Neurological Research, Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada **Intracellular distribution of 3H-delta8-tetrahydrocannabinol in rat organs after i.v. administration.** Research Communications in Chemical Pathology and Pharmacology. 9(1):197-200, 1974.

The intracellular distribution of 3H-delta8-tetrahydrocannbinol (THC) in rat organs after i.v. administration was examined. Much more radioactivity was found in the liver than in the kidney or brain. The drug was almost exclusively associated with particulate fractions in brain. The crude mitochondrial fraction which also contains synaptosomes contained about 50% of the radioactivity. Results show differences in subcellular distribution as well as in binding ability of the drug in the brain and nonneural tissues. It is suggested that the subcellular distribution and binding of THC and/or metabolites in various tissues may be of importance in determining the physiological and pharmacological effects of the drug. 8 references.

195114 Ben-Zvi, Zvi; Bergen, John R.; Burstein, Sumner. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Cannabinol-7-oic acid: a metabolite of delta1-tetrahydrocannabinol in the rhesus monkey.** Research Communications in Chemical Pathology and Pharmacology. 9(1):201-204, 1974.

The effect of cannabinol-7-oic acid in the rhesus monkey is reported. Injection of 14C-delta1-tetrahydrocannabinol (THC) into male rhesus monkeys gave rise to a complex mixture of urinary metabolites. One of these has been isolated and identified as cannabinol-7-oic acid (I). This finding suggests a new metabolic pathway for delta1-THC and raises the possibility that other cannabinol derivatives may also be formed at earlier stages. 5 references. (Author abstract)

195116 Johnson, J. C.; Ratner, M.; Gold, G. J.; Clouet, D. H. New York State Drug Abuse Control Commission, Testing and Research Laboratory, Brooklyn, NY 11217 **Morphine effects on the levels and turnover of catecholamines in rat brain.** Research Communications in Chemical Pathology and Pharmacology. 9(1):41-53, 1974.

The effects of acute and chronic morphine treatment on rat brain catecholamine turnover have been examined. The acute

administration of morphine over a range of pharmacologically effective doses produced slight, transient decreases in norepinephrine levels in most brain areas, and increased rates of norepinephrine biosynthesis in the hypothalamus. In morphine tolerant rats, the changes in norepinephrine turnover were prominent only in the hypothalamus. Morphine effects on dopamine turnover were more pronounced: after acute morphine, striatal dopamine was depleted and turnover rates were increased in most areas of brain, especially in striatum, hypothalamus and midbrain, and after five days of morphine treatment dopamine turnover was increased in all brain areas except cortex. This continuing response in the dopamine system suggests that part of the biochemical adaptation to chronic morphine is an increased synthesis of dopamine. 25 references. (Author abstract)

195117 Karler, Ralph; Cely, William; Turkanis, Stuart A. Department of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **A study of the development of tolerance to an anticonvulsant effect of delta9-tetrahydrocannabinol and cannabidiol.** Research Communications in Chemical Pathology and Pharmacology. 9(1):23-39, 1974.

Tolerance to delta9-tetrahydrocannabinol, cannabidiol, diphenylhydantoin and phenobarbital was studied with a maximal electroshock test in mice. Tolerance to all four drugs developed very rapidly. Hexobarbital sleep times of animals tolerant to delta9-tetrahydrocannabinol and phenobarbital were unchanged; whereas cannabidiol tolerance was accompanied by an increase, and diphenylhydantoin tolerance by a decrease in sleep time. Cross tolerance between the two cannabidiols and diphenylhydantoin and phenobarbital was demonstrable. These results suggest that the mechanism of tolerance to the cannabidiols' anticonvulsant effect in mice is probably dependent upon an adaptation of the central nervous system. 31 references. (Author abstract)

195118 Bolt, A. G.; Mulligan, B. M.; Graham, G. Raymond Purves Research Laboratories, Royal North Shore Hospital, St. Leonards, N. S. W. 2065, Australia **The lipolytic activity of amphetamine in the spinalised cat.** Research Communications in Chemical Pathology and Pharmacology. 9(1):189-192, 1974.

The lipolytic activity of amphetamine in the spinalized cat was examined. Following the i.v. administration of (+)-amphetamine to spinalized cats, levels of free fatty acids in plasma were raised when halothane and chloralase (40mg/kg) were used as anesthetic agents. The results are consistent with the hypothesis that the lipolytic action of amphetamine is not mediated by central activation of the sympathetic nervous system. 4 references. (Author abstract)

195232 Iwata, Heitaroh; Okamoto, Hiroshi; Kuramoto, Ikuko. Department of Pharmacology, Osaka University, Toneyama, Toyonaka, Osaka, Japan **Effect of lithium on serum tryptophan and brain serotonin in rats.** Japanese Journal of Pharmacology (Kyoto). 24(2):235-240, 1974.

The influence of lithium administration on brain serotonin metabolism and the serum tryptophan level in rats was investigated. The brain tryptophan, serotonin and 5-hydroxyindole acetic acid contents did not change after a single injection of lithium, but did increase significantly after repeated injections. A single injection of lithium caused a marked decrease in the serum total tryptophan level, but did not change the ratio of free to albumin bound tryptophan. Repeated injections of lithium caused a significnat increase in serum total tryptophan, and decrease in the ratio of free to bound tryptophan. Addition of lithium ion to normal rat serum in vitro did not change the ratio of free to bound tryptophan. A single injection of lithium produced a marked rise in serum nonesterified fatty acid, which is known to affect the binding of tryptophan by albumin. 19 references. (Author abstract)

195234 Nose, Takashi; Segawa, Tomio. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto, Japan **A comparison of the inhibitory effects of certain antiparkinsonian agents on dopamine accumulation into the rat striatum.** Japanese Journal of Pharmacology (Kyoto). 24(2):299-305, 1974.

The inhibitory effect of certain centrally acting drugs, including antiparkinsonian agents, tricyclic antidepressant and phenothiazine, was studied in vitro on the accumulation of dopamine into a crude mitochondrial fraction (P2-fraction) from rat striatal homogenate, and the site of inhibition was studied by further fractionating the P2-fraction into synaptic vesicles fraction (P2V-fraction) and supernatant fluid (P2S-fraction). Many antiparkinsonian agents, such as benztropine, trihexyphenidyl, ethopropazine, diphenhydramine or 6,6,9-trimethyl-9-azabicyclo(3,3,1)non-3-beta-yl alpha, alpha-di(2-thienyl)glycolate hydrochloride monohydrate (PG-501), inhibited dopamine accumulation into P2-fraction from rat striatal homogenate though atropine did not inhibit the amine accumulation. Benztropine, one of the most potent inhibitors of dopamine accumulation into P2-fraction, inhibited the accumulation into P2V-fraction to a greater extent than that into P2S-fraction and PG-501 inhibited the accumulation into P2S-fraction to a greater extent than that into P2V-fraction. Possible site of action of these two agents is discussed. 10 references. (Author abstract)

195235 Segawa, Tomio; Nakano, Masumi. Department of Pharmacology, Inst. of Pharmaceutical Sciences Hiroshima University School of Medicine, Hiroshima, Japan **Brain serotonin metabolism in lithium treated rats.** Japanese Journal of Pharmacology (Kyoto). 24(2):319-324, 1974.

Brain serotonin metabolism in lithium (Li) treated rats was examined. Five days administration of Li to rats did not significantly alter brain serotonin (5-HT) levels. Animals appeared somewhat sedated but showed considerable exploratory and rearing behavior in new circumstances. Turnover rate of brain 5-HT as measured from the accumulation after inhibiting monoamine oxidase was decreased by repeated administration of Li. Furthermore, Li lessened the depletion rate of brain 5-HT by reserpine. These results suggest that certain of the effects of Li on manic states can be attributed to the reduced functional activity of brain 5-HT neurons. 16 references. (Author abstract)

195236 Krieglstein, J.; Stock, R.; Rieger, H. Pharmakologisches Institut der Universitat Mainz, D-6500 Mainz, Obere Zahlbacher Str. 67, Germany **Influence of therapeutic and toxic doses of neuroleptics and antidepressants on energy metabolism of the isolated perfused rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 279(3):243-254, 1973.

The isolated perfused rat brain was used for a comparative study of the effects of promazine, imipramine, monodesmethyl promazine and desipramine on cerebral energy metabolism. Drug concentrations in the perfusion medium caused a significant decrease of glucose-6-P alone. When the drug concentration was raised to a toxic range reflected in the electroencephalograph by the pattern of secondary discharges, an accumulation of P-creatine and glucose and a decrease of glycogen,

glucose-6-P and ammonia occurred; the lactate/pyruvate ratios remained unchanged. As there were no qualitative differences between the effects of the investigated neuroleptics and antidepressants on cerebral metabolism, it is suggested that these effects might be unspecific and not correlated with the pharmacological action of the drug. 46 references. (Author abstract modified)

195237 Heise, A.; Kroneberg, G. Institut fur Pharmakologie, Bayer AG, D-5600 Wuppertal, Germany **Central nervous system alpha-adrenergic receptors and the mode of action of alpha-methyldopa.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 279(3):285-300, 1973.

Central nervous system alpha-adrenergic receptors and the mode of action of alpha-methyldopa were examined in the cat. Perfusions with alpha-methyldopa, alpha-methyldopamine, alpha-methylnoradrenaline, noradrenaline, or tyramine produced a significant decrease of the systemic arterial blood pressure. The blood pressure lowering effect of the amines was inhibited or abolished by perfusion with phentolamine or yohimbine. In the reserpine pretreated cat the effect of tyramine was strongly inhibited. Perfusions with angiotensin produced an increase of the peripheral blood pressure, while isoprenaline and propranolol showed no significant activity. In the intact anesthetized, as well as in the spinal, cat the intravenous pressor activities of noradrenaline and alpha-methylnoradrenaline were nearly identical. The response of the isolated aortic strip of the rat was somewhat more pronounced to alpha-methylnoradrenaline than to noradrenaline. The results suggest that in the brain stem an alpha-receptor mechanism exists, which is able to mediate a blood pressure decreasing effect of centrally applied catecholamines. 35 references. (Author abstract modified)

195239 Thierry, A. M.; Blanc, G.; Glowinski, J. Groupe NB,(Inserm U. 114), Laboratoire de Biologie Moleculaire, College de France, 11, place Marcelin Berthelot, Paris 5e **Further evidence for the heterogeneous storage of noradrenaline in central noradrenergic terminals.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 279(3):255-266, 1973.

The time course of noradrenaline disappearance has been estimated in the rat cerebral cortex after the injection of FLA 63, an inhibitor of the last step of noradrenaline synthesis. This drug was shown to block 3H-noradrenaline formation from 3H-dopamine within 5 min after its administration. Endogenous levels of noradrenaline decreased in two distinct phases which may correspond to the amine utilization in two compartments, A and B. The compartment A (functional compartment) contained about 20% of the total noradrenaline stores. The turnover rate of noradrenaline in this compartment was estimated to be about seven times that of novadrenaline in compartment B (main storage compartment). The complementarity of the results concerning the rate of noradrenaline synthesis obtained by two different experimental approaches provides further support for the two compartment model of the noradrenaline stores in central noradrenergic terminals. 31 references. (Author abstract modified)

195242 Datta, R. K. Division of Laboratories, Beth Israel Medical Center, New York, NY 10003 **Mescaline-induced changes of brain-cortex ribosomes: effect of mescaline on tRNA and aminoacyl-tRNA synthetase.** Naunyn - Schmiedeberg's Archives of Pharmacology (Berlin). 280(1):107-111, 1973.

In a study of mescaline induced changes of brain cortexribosomes, the effect of mescaline on t-ribonuclic acid (tRNA) and aminoacyl-tRNA synthetase were examined. The pretreatment of brain cortex slices with mescaline does not affect tRNA or aminoacyl-tRNA synthetase, nor have the latter any role in the decreased amino acid incorporating ability of ribosomes of the drug treated slices. 6 references. (Author abstract modified)

195244 Magnusson, Tor. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Effect of chronic transection on dopamine, noradrenaline and 5-hydroxytryptamine in the rat spinal cord.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 278(1):13-22, 1973.

For intervals up to 15 days after transection of the rat spinal cord the level of noradrenaline (NA), dopamine (DA), 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA) and tryptophan were studied above and below the lesions. In the upper part NA, DA and 5-HT increased continuously, while 5-HIAA increased during the first 3 to 5 days and then returned to its original level. In the lower part NA had disappeared almost completely after 15 days, DA after 9 days, 5-HT and 5-HIAA after 5 days. During the first day after transection 5-HT showed an increase in the lower part as did DA for the first 3 days. The different time course for DA and NA suggests that part of the spinal DA serves an independent nonprecursor role. 33 references. (Author abstract)

195245 Hahn, I.; Krieglstein, G.; Krieglstein, J.; Tschentscher, K. Universitat Mainz, D-6500 Mainz, Obere Zahlbacher Strasse 67, Germany **Distribution of chlorpromazine in a simplified blood influenced by various drugs.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 278(1):35-44, 1973.

The binding of chlorpromazine to erythrocytes and to albumin as influenced by other drugs was studied in a simplified blood. Under control conditions 68.1% of chlorpromazine was bound to the erythrocytes, 28.5% was bound to albumin and 3.5% was free in the aqueous phase. The following substances were tested for their ability to alter the distribution of chlorpromazine in the simplified blood: azetazolamide, amitriptyline, chlorimipramine, chlorothiazide, chlortetracycline, desoxycholic acid, diphenylhydantoin, imipramine, indomethacin, ioglycamic acid, oleic acid, oxytetracycline, phenindamine, phenprocoumon, phenylbutazone, probenecid, quinine sulfate, salicylic acid, stearic acid, sulfisoxazole, sulfamethoxypyridazine, suramin, tetracycline, thiopental. In most cases chlorpromazine shifted considerably between erythrocytes and albumin whereas the unbound fraction was not markedly changed. The effect of some of these drugs on the binding of chlorpromazine was also investigated in an albumin solution without erythrocytes. Evidence is presented that the binding capacity of albumin may be fundamentally changed when erythrocytes are presented. It is concluded that binding studies merely with albumin solutions, plasma or serum may be misleading when pharmacokinetic implications are argued. 14 references. (Author abstract modified)

195246 Reinhold, K.; Blasig, J.; Herz, A. Max-Planck-Institut fur Psychiatrie, D-8000 Munchen 40, Kraepelinstrasse 2 and 10, Germany **Changes in brain concentration of biogenic amines and the antinociceptive effect of morphine in rats.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 278(1):69-80, 1973.

The antinociceptive activity of morphine was determined in rats using the vocalisation test, whereby vocalisation was elicited by electrical stimulation of the tail. The effects of various drugs were compared with the corresponding changes in brain amine concentration. Manipulation of 5-hydroxytryp-

tamine (5-HT) levels with parachlorophenylalanine (PCPA) or 5-hydroxytryptophan (5-HTP) did not modify the effect of morphine. Catecholamine (CA) depleting agents antagonized the effect of morphine. Alpha-methyl-p-tyrosine (MT) treatment attenuated the morphine effect and decreased the CA levels, whereas the stimulation threshold before morphine administration was not changed. Inhibition of noradrenaline (NA) synthesis by FLA-63 also reduced the morphine effect. The concentration of morphine in brain was not altered by the alpha-MT treatment. It is suggested that the antinociceptive activity of morphine as tested by this method depends on the concentration of CA in brain, NA being more important than DA. 5-HT does not seem to be involved. 30 references. (Author abstract modified)

195248 Chin, Jane H.; Crankshaw, D. P.; Kendig, Joan J. Department of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305 **Changes in the dorsal root potential with diazepam and with the analgesics aspirin, nitrous oxide, morphine and meperidine.** Neuropharmacology (Oxford). 13(5):305-315, 1974.

The effects of four analgesics and a tranquilizing muscle relaxant were compared on the peripherally evoked dorsal root (D.R.)potential in intact and anesthetized cats. The negative D.R. V component was used as an index of presynaptic inhibition. Diazepam, nitrous oxide, aspirin and meperidine increased the area of D.R. V. However, the effects of the drugs on amplitude and duration differed. Larger doses of diazepam and meperidine decreased the area of D.R. V as did morphine. Anesthesia with nitrous oxide blocked the effects of the analgesics but not those of diazepam. Spinal transection reduced the effects of both diazepam and morphine. The actions of the drugs on the positive D.R. VI component were similar to those on D.R. V except for the effects of aspirin and of small doses of morphine. The results support a possible role for enhancement of presynaptic inhibition in the actions of the drugs tested. 26 references. (Author abstract modified)

195249 Tangri, K. K.; Bhargava, A. K.; Bhargava, K. P. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow, India **Interrelation between monoaminergic and cholinergic mechanisms in the hypothalamic thermoregulatory centre of rabbits.** Neuropharmacology (Oxford). 13(5):333-346, 1974.

The interrelation between monoaminergic and cholinergic mechanisms in the hypothalamic thermoregulatory center of rabbits was examined. The intracerebroventricular injection of acetylcholine, carbachol and physostigmine induced hyperthermia in rabbits while muscarinic agents, pilocarpine and oxotremorine produce a biphasic thermal response consisting of an immediate hyperthermia followed by a delayed hypothermia. An involvement of central nicotinic receptors in the acetylcholine induced hyperthermia is suggested, since it is blocked by intracerebroventricular pretreatment with chlorisondamine and (+)-tubocurarine and not by atropinization. Stimulation of central muscarinic receptors in the hypothalamus are concerned in the delayed hypothermia induced by pilocarpine as it is blocked by prior central atropinization. Intracerebroventricular injection of catecholamines, viz. noradrenaline, adrenaline and dopamine, results in a hyperthermic response due to activation of alpha-adrenoceptors in the hypothalamus, since norepinephrine hyperthermia is blocked by intracerebroventricular pretreatment with phenoxybenzamine and not by propranolol. An interaction between adrenergic and nicotinic mechanisms as well as between tryptaminergic and muscarinic systems is suggested in the hypothalamic thermoregulation in rabbits for the hyperthermic and hypothermic responses, respectively. 37 references. (Author abstract modified)

195250 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire BD7 1DP, England **The importance of the ascending dopaminergic systems to the extrapyramidal and mesolimbic brain areas for the cataleptic action of the neuroleptic and cholinergic agents.** Neuropharmacology (Oxford). 13(5):353-364, 1974.

The relative roles of the extrapyramidal and mesolimbic areas in the catecholaminergic - cholinergic control of catalepsy were investigated by assessment of the effects of disruption to catecholaminergic systems using alpha-methylparatyrosine and by surgical lesion of the ascending dopaminergic pathways to the extrapyramidal and/or mesolimbic brain areas upon neuroleptic and cholinergic catalepsy. Alpha-methylparatyrosine pretreatment was shown to enhance both neuroleptic (haloperidol, fluphenazine, clothiapine, oxypertine and clozapine) and cholinergic (arecoline and RS86) catalepsy. Lesions placed either to interrupt both extrapyramidal and mesolimbic dopaminergic afferents or to interrupt only the innervation to the mesolimbic nuclei caused an initial potentiation followed by a reduction in the cataleptic effects of the neuroleptic agents but caused potentiation of cholinergic catalepsy at all times of testing. The results are interpreted as supporting a dopaminergic - cholinergic balanced control of catalepsy which involves not only the extrapyramidal but also the mesolimbic dopaminergic systems. 31 references. (Author abstract)

195252 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, 7, Yorkshire, England **The site of and mode of action of ET495 for the mediation of stereotyped behaviour in the rat.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 278(2):117-133, 1973.

The role of catecholaminergic systems in the mediation of ET495 stereotyped behavior was investigated using agents known to modify presynaptic events. Pretreatment with the benzoquinolizine derivatives tetrabenazine and Ro 04-1284 and the indole derivatives oxypertine and solypertine, agents considered to exert their effects via depletion of catecholamines from the terminal storage granules, was found to reduce or abolish the stereotypic effects of ET495. Inhibition of the synthesis of catecholamines at the tyrosine hydroxylation stage using alpha-methyl-para-tyrosine was also found to reduce or abolish the effect of ET495. In the brain lesion studies it was found that the stereotypic effects of ET495 were completely abolished both during the acute and chronic stages following ablation of the ascending dopaminergic fibers to both the extrapyramidal and mesolimbic systems in the lateral hypothalamus. Destruction of the dopaminergic fibers at the level of the rostral hypothalamus, which supply only the mesolimbic systems, abolished all components of stereotypy during the acute phase, but only abolished the weaker intensity components during the chronic stage. 26 references. (Author abstract modified)

195254 Schultz, Joachim; Hamprecht, Bernd. Institut fur Toxicologie der Universitat, D-7400 Tubingen, Lothar-Meyer-Bau, Wilhelmstrasse 56, Germany **Adenosine 3',5'-monophosphate in cultured neuroblastoma cells: effect of adenosine, phosphodiesterase inhibitors and benzazepines.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 278(2):215-225, 1973.

The effect of various neurohormones on intracellular levels of adenosine 3',5'-monophosphate were evaluated in a neuroblastoma cell line both, in the presence and in the absence of the phosphodiesterase inhibitors isobutylmethylxanthine and papaverine. Without the phosphodiesterase inhibitors only prostaglandin E1 increased intracellular adenosine 3',5'-monophosphate levels. In the presence of isobutylmethylxanthine and/or papaverine, however, adenosine stimulated adenosine 3',5'-monophosphate formation and the effect of prostaglandin E1 was greatly potentiated. Treatment of the cells with dopamine, 5-hydroxytryptamine, noradrenaline, adrenaline, histamine and prostaglandin F1alpha was without effect on adenosine 3',5'-monophosphate levels either in the presence or absence of the phosphodiesterase inhibitors. The effect of adenosine was not antagonized by theophylline. Several adenosine analogs were tested and found to have little or no effect on adenosine 3',5'-monophosphate levels in neuroblastoma N4TG3. Diazepam and to a lesser extent chlordiazepoxide act like phosphodiesterase inhibitors when incubated together with prostaglandin E1. 29 references. (Author abstract modified)

195429 Anden, Nils-Erik; Strombom, Ulf. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Adrenergic receptor blocking agents: effects on central noradrenaline and dopamine receptors and on motor activity.** Psychopharmacologia (Berlin). 38(2):91-103, 1974.

The effects of alpha adrenergic blocking agents on the central noradrenaline and dopamine receptors and on motor activity were examined. Phenoxybenzamine, but not phentolamine or propranolol, blocked central noradrenaline receptors in flexor reflex experiments on the rat spinal cord using the selective noradrenaline receptor stimulating agent clonidine. None of these three drugs blocked dopamine receptors in experiments on turning of unilaterally striatectomized rats induced by the dopamine receptor stimulating agent apomorphine. The alpha-methyltyrosine induced disappearance of noradrenaline in the central nervous system of rats and mice was accelerated by phenoxybenzamine at doses related to the functional changes, whereas the other drugs were inefficient. Phentolamine and propranolol reduced the stimulation seen both after apomorphine alone and in combination with clonidine, indicating nonspecific sedative effects. Phentolamine blocked the peripheral effects of clonidine but did not markedly diminish the activation induced by the receptor stimulants. Phenoxybenzamine blocked the clonidine induced potentiation without interfering with the apomorphine induced stimulation and can thus be used as a blocking agent of central and peripheral noradrenaline receptors in behavioral experiments. 31 references. (Author abstract modified)

195436 Simpson, Lance L. Department of Pharmacology, College of Physicians and Surgeons, Columbia University, 630 West 168th St., New York, NY 10032 **The effects of lithium and physostigmine on rat brain acetylcholinesterase activity.** Psychopharmacologia (Berlin). 38(2):145-150, 1974.

The anticholinesterase activity of lithium and physostigmine have been investigated. It was found that lithium had no anticholinesterase activity in vivo and slight anticholinesterase activity in vitro. The latter effect was evident only under markedly unphysiological conditions, i.e.,concentrated lithium and dilute acetylcholinesterase. It was also found that repeated injections of physostigmine did not result in tolerance to the anticholinerase effects of the drug. A single challenge dose of physostigmine or a series of concentrations of physostigmine resulted in similar inhibition of AChE from animals which had or had not received a 5 day regimen of repeated physostigmine injections. The relationship of these findings to the treatment of mania is discussed. 7 references. (Author abstract modified)

195437 Tonge, Sally R. School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF, England **Noradrenaline and 5-hydroxytryptamine metabolism in six areas of rat brain during post-amphetamine depression.** Psychopharmacologia (Berlin). 38(2):181-186, 1974.

Noradrenaline and 5-hydroxytryptamine metabolism were studied in six areas of rat brain during postamphetamine depression. Mature male Wistar rats were given d-amphetamine sulphate in the drinking water for a period of 3 weeks. The drug was then withdrawn and the rats were killed 12, 24, 36 and 48 h later. Pronounced behavioral depression was observed 12 h after the withdrawal of amphetamine; 24 h after withdrawal, behavior was substantially normal but depression recurred at 36 h. Recovery appeared to be complete after 48 h. Fluorimetric determinations showed that noradrenaline and 5-hydroxytryptamine concentrations were reduced by the chronic administration of amphetamine in the cortex, hippocampus, thalamus/hypothalamus and midbrain. Noradrenaline concentrations were also reduced in the pons/medulla. Twelve and 36 h after withdrawal, there was a further reduction in noradrenaline concentrations in the cortex, hippocampus and midbrain; noradrenaline concentrations in the striatum were also reduced. 13 references. (Author abstract modified)

195438 Stone, T. W. Department of Physiology, University of Aberdeen, Marischal College, Aberdeen, Scotland **Pharmacology of pyramidal tract cells in the cerebral cortex: noradrenaline and related substances.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 278(4):333-346, 1973.

Noradrenaline and pharmacologically related substances were applied to identified pyramidal tract cells in the cerebral cortex of rats anesthetized with urethane. A total of 64% of these cells were depressed by noradrenaline, and this response could be potentiated by iproniazid..Noradrenaline could be blocked occasionally by phentolamine and more frequently by propranolol, and was mimicked closely by isoprenaline; alpha-methylnoradrenaline had only a weak depressant action. This specific blockade of noradrenaline depression suggests that noradrenaline may be acting on receptors resembling beta-receptors in the periphery, and that the depressions do not represent a nonspecific depression by noradrenaline of the neuronal membrane. No correlation between cells responding to noradrenaline and cells responding to thalamic, transcallosal or epicortical stimulation occurred. Noradrenaline is therefore concluded not to be a transmitter in pathways from these sites. 33 references. (Author abstract modified)

195439 Stock, Gunter; Magnusson, Tor; Anden, Nils-Erik. Physiologisches Institut der Universitat Heidelberg, D-6900 Heidelberg, Germany **Increase in brain dopamine after axotomy or treatment with gamma-hydroxybutyric acid due to elimination of the nerve impulse flow.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 278(4):347-361, 1973.

Both a unilateral, frontal section of the rat brain at the level of the caudal hypothalamus and systemic treatment with gamma-hydroxybutyric acid (GHBA, sodium form) increased the dopamine (DA) in the forebrain by about 70% in 1 hour and decelerated the alpha-methyltyrosine induced DA disappearance. Brain noradrenaline was significantly lowered after the hemisection but was not influenced by GHBA given either

alone or in combination with alpha-methyltyrosine. Intrastriatal injections of KCl did not change normal DA content significantly but prevented the increase in DA observed after hemisection or GHBA treatment; they also rapidly released the DA accumulated after hemisection. The same increase in forebrain DA was also seen after injections of 25% KCl into the substantia nigra or tetrodotoxin into the neostriatum. Unilateral injections of the KCl into the neostriatum depolarized cells whereas stimulation of the DA receptors hyperpolarized them. Increases in brain DA may be due to inhibition of the nerve impulse flow to the DA nerve terminals. 41 references. (Author abstract modified)

195440 Anden, Nils-Erik; Magnusson, Tor; Stock, Gunter. Department of Pharmacology, University of Goteborg, Fack, S-400 33, Goteborg 33, Sweden **Effects of drugs influencing monoamine mechanisms on the increase in brain dopamine produced by axotomy or treatment with gamma-hydroxybutyric acid.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 278(4):363-372, 1973.

The influence of blockage or stimulation of dopamine (DA) receptors on the selective increase in brain DA seen after axotomy or injection of gamma-hydroxybutyric acid (GHBA) was studied in rats. Increases were not changed after blockade by haloperidol but were slightly reduced after stimulation by apomorphine. Since pretreatment with haloperidol counteracted apomorphine's effect, a diminished stimulation of DA receptors may be partially responsible for increase in brain DA seen when the nerve impulse flow has been blocked in the DA neurons by axotomy or treatment with GHBA. Increase in brain DA usually observed after axotomy was not found with treatment with reserpine and nialamide, suggesting that the negative feedback of cytoplasmic DA on the DA synthesis operates also in the absence of nerve impulses. Amphetamine injection before or after axotomy or treatment with GHBA markedly inhibited brain DA increase, probably due to release of newly synthesized DA. 21 references. (Author abstract modified)

195441 Philippu, A.; Roensberg, W.; Przuntek, H. Institut fur Pharmakologie und Toxikologie der Universitat, D-8700 Wurzburg, Koellikerstrasse 2, Germany **Effects of adrenergic drugs on pressor responses to hypothalamic stimulation.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 278(4):373-386, 1973.

The posterior area of the hypothalamus of anesthetized cats were superfused with artificial cerebrospinal fluid through a push - pull cannula. Overall data indicate that: (1) alpha-adrenoreceptors are present in the posterior hypothalamus and are involved in blood pressure rise elicited by its electrical stimulation; (2) a feedback mechanism is present in the hypothalamus which regulates the increase of noradrenaline and which is mediated by alpha-adrenoreceptors; inhibition of the release leads to an enhanced release of the neurotransmitter; (3) activation of the inhibitory pathways of the nucleus of the solitary tract by clonidine diminishes the pressor response to electrical stimulation of the hypothalamic posterior area; (4) two adrenergic systems localized in different areas of the central nervous system oppose each other in their regulatory effects on arterial blood pressure. 16 references. (Author abstract modified)

195448 Agarwal, M. K. INSERM U-36, 17 Rue de Fer-a-Moulin, Paris 75005, France **Analysis of the influence of selected neurotropic agents on hepatic metabolism in relation to endotoxicosis.** Biochemical Pharmacology (Oxford). 23(18):2577-2584, 1974.

A number of neurotropic agents were tested in rats for influence on hepatic metabolism in relation to their ability to alter sensitivity to bacterial endotoxin which is known to derange both neurotransmission and also the homeostasis of selected functions in the liver. Like endotoxin, dihydroxyphenylalanine (DOPA) lowered hepatic tryptophan pyrrolase (TP) activity within 6 hr and this effect was specific since neither of the two other analogs parachlorophenylalanine (PCPA) and phenylalanine, nor serotonin and LSD-25, depressed the hepatic TP. The LSD-25 or PCPA, but not phenylalanine, DOPA or serotonin, increased hepatic tyrosine transaminase (TT). Contrary to endotoxin, neither agent lowered liver glycogen levels in 4 hr but these decreased 18 hr after phenylalanine or LSD-25. The organic mercurial p-chloromercuribenzoate (which only minimally alters endotoxin toxicity) was less toxic than HgCl2 for these hepatic functions. The uptake and distribution of cortisone were not altered by either mercurial. 18 references. (Author abstract modified)

195449 Jonsson, Gosta; Lohmander, Stefan; Sachs, Charlotte. Department of Histology, Karolinska Institutet, S-104 01, Stockholm 60, Sweden **6-Hydroxydopamine induced degeneration of noradrenaline neurons in the scorbutic guinea-pig.** Biochemical Pharmacology (Oxford). 23(18):2585-2593, 1974.

The effect of the neurotoxic compound 6-hydroxydopamine and its immediate precursor 6-hydroxy-DOPA on noradrenaline (NA) uptake and storage in central and peripheral catecholamine neurons of scorbutic and normal guinea-pigs has been investigated. Endogenous noradrenaline in heart and brain as well as the in vitro uptake - accumulation of 3H-noradrenaline in iris and slices of heart and brain were not significantly changed in scorbutic animals. The in vitro formation of 3H-noradrenaline from 3H-dopamine was markedly reduced in heart slices of scorbutic guinea-pigs, due to ascorbic acid's being a cofactor for dopamine-beta-hydroxylase. There was increased depletion of brain noradrenaline following tyrosine hydroxylase inhibition produced by alpha-methyl-p-tyrosine methylester in scorbutic animals, indicating an increased NA turnover. Administration of 6-hydroxydopamine or 6-hydroxy-DOPA resulted in a similar reduction of endogenous NA in brain and heart as well as of the in vitro uptake of 3H-noradrenaline in iris, and slices from heart, cerebral cortex and hypothalamus in scorbutic and control guinea-pigs. These results are discussed in view of current hypotheses on mechanisms involved in the neurotoxic action of 6-hydroxydopamine on catecholamine neurons. 31 references. (Author abstract)

195450 Goode, David J.; Meltzer, Herbert Y. Department of Psychiatry, University of Chicago Hospitals and Clinics, Chicago, IL 60637 **Cytotoxic effects of imipramine on platelets.** Biochemical Pharmacology (Oxford). 23(18):2629-2635, 1974.

The cytotoxic effects of imipramine on platelets were examined. Incubation for 30 min at 30 degrees with 1 mM imipramine, chlorpromazine or phencyclidine produced increases in creatine phosphokinease (CPK) activity of rat platelet rich plasma (PRP). Increases in lactic dehydrogenase (LDH) activity of human PRP were produced by imipramine at 0.5mM. Ouabain, diphenylhydantoin, calcium chloride, EDTA and thrombin did not effect CPK activity of rat PRP. None of the drugs tested except 10 mM diphenylhydantoin affected CPK or LDH activity in platelet poor plasma. Increases in enzyme activity of PRP produced by 1 mM imipramine were associated with a decrease in platelet count. The increases were independent of temperature of incubation from 0 degrees to 30 degrees and were maximal after a 5 min incubation. The

release of LDH and CPK caused by the above drugs is not related to platelet aggregation or the platelet release reaction. The increases in LDH and CPK activity in PRP appear to be the result of platelet destruction or damage to the platelet membrane with release of these enzymes. 30 references. (Author abstract)

195539 Johansson, J. O.; Jarbe, T. U. C.; Henriksson, B. G. Department of Psychology, University of Uppsala, Slottsgrand 3 S-752 20 Uppsala, Sweden **Physostigmine attentuation of delta9-tetrahydrocannabinol induced hyperthermia in rats.** Experientia (Basel). 30(7):779-780, 1974.

The attenuation of delta9-tetrahydrocannabinol (THC) induced hyperthermia by physostigmine was studied in rats. It was hypothesized that equimolar doses of neostigmine would indicate whether the THC hyperthermia was of central or peripheral origin. It was concluded that, although morphine and THC produce similar thermal effects, the underlying mechanisms need not necessarily be the same. 14 references.

195540 Marcy, R.; Quermonne, M. A. Department of Pharmacology, University of Caen, 1, rue Vaubenard, F-14032 Caen-Cedex, France **Anhydrotic effect of benzodiazepines in mice.** Experientia (Basel). 30(7):783-784, 1974.

The inhibitory effect of benzodiazepines on palmar sweating in mice was studied. The anhydrotic effect was assessed by the inhibition of palmar skin conductibility (IPSC). It was found that administration of benzodiazepines to mice resulted in IPSC secondary to an inhibition of sweating and that the IPSC is dose dependent. The different mechanisms (cholinergic, adrenergic, and central) that may be involved in this inhibition are discussed. 12 references.

195548 Bhargava, Vinod. Department of Pharmacology, H.P. Medical College, Simla (H.P.), India **Blockade by eserine of the cerebral cortical effects of alloferin: a further evidence of cholinergic inhibitory mechanism.** Japanese Journal of Pharmacology (Kyoto). 24(1):1-4, 1974.

Blockade by eserine of the cerebral cortical effects of alloferin is reported. In rats anesthetised with pentobarbitone, somatosensory evoked potentials, produced by stimulation of contralateral or ipsilateral forepaws were used to measure the activity in different neuronal pathways. Computer derived averages of 32 consecutive responses yielded a stable and conistent measurement of the evoked potentials. The drugs were applied to the cerebral cortex by using cortical cup technique and changes were measured in evoked potentials. Cortical application of alloferin increased the amplitude of the early negative wave of the cortical evoked potentials. This effect of alloferin was blocked by prior treatment of the cortex with eserine. It appears that the excitant effect of aloferin on the cortex was the result of disinhibition of cortical cholinergic inhibitory mechanism. 8 references. (Author abstract)

195549 Fukuda, Naohisa; Saji, Yoshiaki; Nagawa, Yuji. Biological Research Laboratories, Takeda Chemical Industries, Ltd., Higashiyodogawa-ku, Osaka, Japan **Neuropharmacological studies of effect of new central depressant, 8-chlor-6-phenyl-4H-s-triazolo (4,3-a) 1-4) benzodiazepine (D4OTA) on EEG and central sympathetic activating mechanism in cats.** Japanese Journal of Pharmacology 24(1):75-88, 1974.

The effects of 8-chloro-6-phenyl-4H-s-triazolo (4, 3-a) (1-4) benzodiazepine (D-40TA) on the electroencephalogram (EEG) arousal and sympathetic excitatory responses evoked spontaneously or by stimulation of the midbrain reticular formation, posterior hypothalamus, thalamus and sciatic nerve in the curarized, intact brain or cerveau isole cats provided the following conclusion: D-40TA reduced structures, and limited the persistence of the EEG arousal by selective depression component with much less influence upon a phasic EEG component related to waking ability itself. These dual effects may be responsible for hypnogenic action of D-40TA. 26 references. (Author abstract)

195591 Serck-Hanssen, Guldborg. Institute of Physiology, University of Bergen, 5000 Bergen, Norway **Effects of theophylline and propranolol on acetylcholine-induced release of adrenal medullary catecholamines.** Biochemical Pharmacology (Oxford). 23(16):2225-2234, 1974.

The effect of theophylline and propranolol on acteylcholine induced catecholamine release was studied in isolated bovine adrenals perfused in vitro. The catecholamine release was potentiated about 140% by the presence of 1 mM theophylline in the perfusion medium. Theophylline enhanced the release of adrenaline but had little effect on the release of noradrenaline. The augmentary effect of theophylline on the adrenaline release was partially reduced by 0.1micromolar atropine and by 1.0micromolar propranolol. Propranolol by itself at a concentration of 0.1micromoles at which it had no membrane stabilizing effect, reduced the acetylcholine induced secretion about 20%. It is concluded that theophylline affected the release of adrenaline by mobilization of intracellular calcium stores and by preventing breakdown of cyclic-AMP synthesized in response to stimulation of a beta-adrenergic receptor located in the adrenaline storing cells. A possible action of theophylline on cyclic guanosine 3',5'-monophosphate synthesized in response to stimulation of the muscarinic receptor is discussed. 35 references. (Author abstract modified)

195907 Corcoran, Michael E.; Fibiger, Hans C.; McCaughran, James A., Jr.; Wada, Juhn A. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, B.C., V6T 1W5, Canada **Potentiation of amygdaloid kindling and Metrazol-induced seizures by 6-hydroxydopamine in rats.** Experimental Neurology. 45(1):118-133, 1974.

Potentiation of amygdaloid kindling and Metrazol induced seizures by 6-hydroxydopamine (6-OHDA) was investigated in rats. Control rats responded to the subcutaneous injection of pentylenetetrazol (Metrazol) with one or more brief intermittent clonic convulsions. In contrast, the rats pretreated with 6-OHDA displayed significantly longer episodes of generalized seizures, nearly all of which contained episodes of tonic extension of the hindlimbs. The severity of the seizure syndrome in rats with substantial depletion of both norepinephrine (NE) and dopamine (DA) did not differ markedly from that in rats with preferential depletion of NE, suggesting that depletion of NE, and not DA, is the mechanism of the exacerbated convulsive response to Metrazol produced by 6-OHDA. The data suggest that combined destruction of noradrenergic and dopaminergic neurons, or destruction of the latter alone, is necessary to facilitate the development of kindled seizures. Together, the two experiments confirm earlier obsrvations that central catecholaminergic systems tend to inhibit a variety of seizure phenomena. 46 references. (Author abstract modified)

195950 Lindqvist, Margit; Kehr, Wolfgang; Carlsson, Arvid. Dept. of Pharmacolgy, Fack, S-40033 Goteberg 33, Sweden **Effect of pentobarbitone and diethyl ether on the synthesis of monoamines in rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(3):263-277, 1974.

The effect of pentobarbitone and diethyl ether on the synthesis of monoamines in rat brain was investigated. Pentobarbitone retarded the formation of dopa and 5-hydroxytryptophan (5-HTP) by about 25% in most brain regions but had no effect on striatal dopa formation. Ether accelerated the formation of dopa and 5-HTP in most brain regions, the action on striatal dopa being most pronounced. The effect was generally somewhat less marked during the second than during the first half hour of anaesthesia. A postanaesthetic inhibition of dopa formation was found in the striatum and of 5-HTP formation in whole brain. If hypothermia was allowed to develop, the stimulating action of ether on dopa and 5-HTP formation tended to be partly antagonized. A complex interaction between 3-hydroxybenzylhydrazine HCL (NSD 1015) and the hypothermic response to ether was observed. 21 references. (Author abstract modified)

195992 Capobianco, Salvatore; Mountford, Damon. Dept. of Psychology, Rutgers Univ., New Brunswick, NJ 08903 **The effects of drug administration to the lateral hypothalamus: neurochemical coding or nonspecificity?** Bulletin of the Psychonomic Society. 3(3A):179-180, 1974.

Adrenergic and cholinergic drugs were utilized to investigate receptor specificity in the lateral hypothalamic feeding and drinking systems in the rat. Natural hunger was not effectively reduced by adrenergic antagonism. Cholinergic agents elicited and blocked eating responses under different conditions. The results are interpreted as a lack of specificity and are discussed in terms of such a model. 12 references. (Author abstract)

196025 Middaugh, Lawrence D.; Blackwell, L. Ann; Santos, Carroll A., III; Zemp, John W. Dept. of Biochemistry, Medical Univ. of South Carolina, 80 Barre St., Charleston, SC 29401 **Effects of d-amphetamine sulfate given to pregnant mice on activity and on catecholamines in the brains of offspring.** Developmental Psychobiology. 7(5):429-438, 1974.

A study to determine the effects of d-amphetamine sulfate given to pregnant mice on the activity and on catecholamines (CA) in the brains of the offspring is reported. Offspring of C57BL/6J injected during the last trimester of pregnancy had slightly reduced bodyweight at birth, altered concentrations of CA in their brains during development and increased activity after they matured. Norepinephrine concentrations were depressed at birth, returned to control values by day three and were elevated at 21 and 30 days after birth. Dopamine values were elevated at 30 days after birth. At 75 days of age, animals prenatally exposed to the drug had CA concentrations similar to controls but had heightened activity levels compared to controls tested in open field. Results showed that d-amphetamine sulfate administered to mice during the last third of pregnancy produced transient alterations in CA concentrations and long-lasting changes in behavior. 27 references. (Author abstract modified)

196107 Quest, J. A.; Rowles, G. S.; Mulligan, L. T.; Mathur, P. P. Bureau of Drugs, Div. of CarioRenal Drug Products, Food and Drug Adm., Rockville, MD 20852 **Mechanism of the hypotensive effect of intravenous methaqualone in the cat.** Toxicology and Applied Pharmacology. 29(3):420-433, 1974.

The mechanism of the hypotensive effect of intravenous methaqualone was investigated in the cat. In chloralose anesthetized cats, iv administration of methaqualone produced dose dependent decreases in blood pressure. The hypotension was associated with decreases in contractile force and heartrate at doses of 1mg/kg or higher. In vagotomized cats, spinal section markedly reduced the depressant effects of methaqualone on blood pressure, and contractile force and heartrate and removal of the stellate ganglia reduced the inotropic and chronotropic effects. In the isolated cat hindquarters preparation perfused at constant blood flow, methaqualone produced transient decreases in perfusion pressure which were not altered by pretreatment with phentolamine, propranolol, atropine or tripelennamine. A centrally mediated depression of sympathetic neural outflow to the heart and vasculature and direct relaxation of vascular smooth muscle and direct myocardial depression are suggested as causes of methaqualone hypotension. 20 references. (Author abstract modified)

196250 Kearse, Bettye C. Wilson. New York University **The effect of psychopharmacological drugs on puffing and on RNA and DNA syntheses in the salivary gland chromosomes of Drosophila melanogaster. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-1909 HC$12.50 MF$4.00 84 p.

The effects of the psychotropic drugs, caffeine, diethazine, chlorpromazine, and mescaline, on the activity of loci in the salivary gland chromosomes of Drosophila melanogaster larvae were investigated. Three third instar ages were used to examine the possibility that response of the genetic material, ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), is related to the age of the organisms. Glands were excised from larvae 110, 115, and 120 hours after egg fertilization and were incubated in the psychoactive drugs, in insect Ringer's solution, in Actinomycin D, or in ecdysterone. Each treatment was followed by an incubation in H3U or H3T. Glands were then fixed, squashed, stained, photographed and scored for puff size. Slides were prepared for autoradiography to assess the effect of the solutions on RNA and DNA syntheses. Findings indicate that the salivary gland chromosomes of the larvae do interact during development with external agents, including psychotropic drugs, exogenous ecdysterone, and Actinomycin D. (Journal abstract modified)

196256 Saunders, Donald Roy. Purdue University **Age-related enhanced responsiveness to central nervous system drugs in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-5046 HC$12.50 MF$4.00 87 p.

Age related alterations in the responsiveness of mature rats to centrally acting drugs, sodium hexobarbital, chlorpromazine hydrochloride, morphine sulfate, and d-amphetamine sulfate were studied. The iv infused dose of hexobarbital required to suppress EEG activity for 1 sec was lower in older (9 to 10 month-old) Ss than in 2.5to 3-month-old Ss. Chlorpromazine produced a greater hypothermia in older Ss at the end of 2.5hr. Dose - response curves for morphine analgesia were different in the two age groups as measured by footshock induced vocalization. The slope of the dose - response curve for amphetamine stimulated motor activity was significantly steeper for older Ss. Results indicate that the responsiveness of rats to these centrally acting drugs increases with age, clearly demonstrating the importance of age as a factor in preclinical drug evaluation studies. (Journal abstract modified)

196259 Sinclair, John Gordon. Purdue University **The effects of diphenylaminoethanol (DPAE) and lidocaine on cerebellar inhibition Deiters neurons. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-4912 HC$12.50 MF$4.00 71 p.

The effects of diphenylaminoethanol (DPAE) and lidocaine on cerebellar inhibition of Deiters' (lateral vestibular) neurons were examined in cats to determine if they would antagonize the Purkinje cell inhibition of Deiters' units. The data from intracellular tests indicate that DPAE failed to block the inhibition and suggest that DPAE is not a potent gamma-aminobutyric acid (GABA) antagonist. The effects of lidocaine were not consistent. Cerebellar inhibition of Deiter's neurons was decreased in some intracellular experiments, but generally the antagonism was not marked. Conversely, in extracellular experiments, lidocaine produced a surprisingly large mean increase of 350% in the cerebellar threshold voltage required to inhibit the activation of Deiters' neurons by vestibular nerve stimulation. It is felt that, since GABA has been implicated as the inhibitory transmitter at the Purkinje cell - Deiter's neuron synapse, iontophoretic studies should be performed to study the effects of lidocaine on the GABA mediated inhibition. 6 references. (Journal abstract modified)

196261 Schaub, Robert George. Washington State University **Involvement of serotonin in hyperkinetic episodes in Scottish terrier dogs. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-4128 HC$12.50 MF$4.00 78 p.

The involvement of serotonin (5-HT) in an inherited neuromuscular disorder in Scottish terrior dogs was investigated, and the effect of certain drugs which alter the severity of the disease on apparent central nervous system serotonin concentration was assessed. Apparent central nervous system concentrations were determined by measuring the concentration of the major serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid. Drugs tested included nialamide, a potent monamine oxidase inhibitor, parachlorophenylalanine, an inhibitor of the rate limiting step in serotonin synthesis, and 5-hydroxytryptophan, the immediate precursor of 5-HT. Serotonin content in brain and whole blood and 5-hydroxyindoleacetic acid concentration in cisternal cerebrospinal fluid were determined in normal dogs and diseased ones, as well as increases in the fluid 5-HIAA following p-chlorophenylalanine administration. No significant differences between the two groups of Ss occurred. (Journal abstract modified)

196580 Gardey-Levassort, C.; Olive, G.; Lechat, P. Institut de Pharmacologie, 21, rue de l'Ecole-de-Medecine, F-75270 Paris, Cedex 06, France **Action of probenecid on the central nervous system of the rabbit: II. Potentiation of 5-hydroxytryptophan-induced hyperthermia and suppression of this effect by a decarboxylase inhibitor (Ro4-4602).** Pharmacology. 11(5):268-277, 1974.

The action of probenecid on the central nervous system was studied in the rabbit. In rabbits pretreated with i.p. probenecid, the hyperthermia induced by 5-hydroxytryptophan (5-HTP) was markedly potentiated. There was no change in the level of 5-hydroxytryptamine (5-HT) in the hypothalamus and brainstem. There was no direct relation in this situation between hyperthermia and the cerebral levels of 5-HT. High doses of N1(D,L-seryl)-N2-(2,3,4-trihydroxybenzyl)-hydrazine (Ro4-4602) inhibited the hyperthermic effect of 5-HTP and of 5-HTP in the presence of probenecid, although the levels of 5-HT in the hypothalamus and brainstem were elevated. At the same time, a decrease in the concentration of 5-hydroxyindolacetic acid was observed in the cerebrospinal fluid. It was suggested that Ro4-4602 may inhibit the abnormal synthesis of 5-HT induced by an excess of 5-HTP in hypothalamic thermoregulatory structures other than 5-hydroxytryptaminergic structures. 26 references. (Author abstract modified)

196582 Florez, J. Departmento de Farmacologia, Facultad de Medicina, Universidad de La Laguna, Tenerife, Canary Islands, Spain **The site of the respiratory stimulant action of imidazole in cats.** Pharmacology. 11(5):308-315, 1974.

The analeptic activity of imidazole was studied in cats. The drug was injected systemically, into the vertebral artery and into the third ventricle of decerebrate and/or anesthetized cats. Respiratory stimulation was consistently induced by all routes even in animals deprived of peripheral chemoreceptors. The duration of the stimulation varied from 30 to 90 min. The action seemed to be located at the medullopontine centers although the hypothalamus may also be involved. Convulsant action of imidazole was observed in decerebrate cats after intravenous administration and in intact anesthetized cats after injection of the drug into the third ventricle. 14 references. (Author abstract)

196588 Zivkovic, B.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, St. Elizabeths Hospital, Washington, DC 20032 **Tyrosine hydroxylase (TH) in N. accumbens and striatum: effects of neuroleptics on the affinity for pteridine cofactor. (Unpublished paper).** Washington, D. C., NIMH, 1974. 1 p.

The effects of neuroleptics on the affinity for pteridine cofactor in N. accumbens and striatum were studied. The injection of various neuroleptics decreased the apparent Km of striatal tyrosine hydroxylase (TH) for pteridine cofactors (DMPH4 and 6MPH4) without affecting the Vmax. This kinetic change increased TH activity when the enzyme was measured in the presence of unsaturating concentration of the cofactor. Haloperidol, pimozide and chlorpromazine increased, at 30 min postinjections, the striatal TH activity by 50%. The doses required to produce a similar increase in TH activity of accumbens were two to six times greater. Clozapine and thioridazine increased the TH activity in accumbens about 50%, double the dose necessary for the striatum. It appeared that the liability for extrapyramidal side-effects was greater when neuroleptics selectively activated TH of striatum. (Author abstract modified)

196590 Hanbauer, I.; Guidotti, A.; Costa, E. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Involvement of cyclic nucleotides in the long term induction of tyrosine hydroxylase. (Unpublished paper).** Washington, D.C., NIMH, 1974. 30 p.

The involvement of cyclic nucleotides in the long-term induction of tyrosine hydroxylase (TH) in rats is reported. In adrenal medulla, the immediate response to application of various stimuli which trigger an increase of TH activity is manifested by an increase of 3',5'-cyclic adenosine monophosphate (cAMP) concentrations. The extent and duration of this increase plays a fundamental role in the TH induction triggered by stimulation of nicotinic receptors. In sympathetic ganglia, several types of mechanisms exist by which an induction of TH can be brought about. Cold exposure and injection of reserpine did not alter the cAMP content in superior cervical ganglia (SCG) but did trigger TH induction. Cold exposure of adrenal demedullated rats resulted in an immediate rate increase of cAMP concentration, a long-lasting elevation of plasma corticosteriod levels and a delayed TH induction if SCG. Nicotinic receptor blockers, decentralization and propranolol prevented the rise in cAMP content and TH activity. (Author abstract modified)

196593 Bonnay, Marc M.; Guerinot, Francoise; Bohuon, Claude J. Institut Gustave-Roussy, 16bis, Avenue P.-Vaillant-

Couturier, 94-Villejuif (Val-de-Marne), France **Evidence for a peripheral effect of fusaric acid, a dopamine beta-hydroxylase inhibitor, on serotonin metabolism.** Biochemical Pharmacology (Oxford). 23(19):2770-2773, 1974.

The extracerebral and the intracerebral tryptophan metabolism in the rat was investigated simultaneously after treatment by dopamine-beta-hydroxylase (DH) and the mechanisms of action of fusaric acid and 1-phenyl-3-(2-thiazolyl)-2-thiourea (U-14,624) were compared. It is concluded that fusaric acid acts in two ways on the metabolism of 5-hydroxytryptamine (5-HT) a central effect common to most DBH inhibitors and a peripheral ef action due to the inhibition of the binding of tryptophan to serum albumin. The inhibitory effect of U-14,624 and fusaric acid on DBH was shown by a sharp drop in the brain norepinephrine concentrations. Both drugs increased tryptophan, 5-hydroxyindoleacetic acid, and 5-HT concentrations in the brain. Fusaric acid increased the blood free tryptophan concentration. Results are discussed and compared with other studies. 10 references.

196782 Kohut, A.; Nicak, A. Lekarska fakulta UPJS, Katedra farmokologie, Kosice, Srobarova 57, Czechoslovakia **Relationship between analgesic action of pethidine and its effect on the brain 5-hydroxytryptamine concentration in the rats of different age.** Activitas Nervosa Superior (Praha). 16(2):130-133, 1974.

The relationship between the analgesic action of pethidine and its effect on the concentration of 5-hydroxytryptamine (5-HT) in the brain of rats of different ages was studied. 20mg/kg of pethidine injected intraperitoneally increased the pain threshold 20 minutes after its injection in 12 day, 3 and 18-month-old rats. In 50 minutes, its analgesic action was noted in the groups of 3 and 18-month-old rats. Eighty minutes after administration, no analgesic action was observed. Pethidine significantly decreased 5-HT in the brain in all age groups and in all time intervals. It is suggested that age dependent differences in the analgesic action of pethidine are not accompanied by age dependent changes of 5-HT in the brain of rats. Pethidine decreased concentration of 5-HT in the brain also when analgesic action was not observed. 16 references. (Author abstract modified)

196800 Benjamin, A. M.; Quastel, J. H. Div. of Neurological Sciences, Dept. of Psychiatry, Univ. of British Columbia, Vancouver V6T 1W5, BC, Canada **Fate of L-glutamate in the brain.** Journal of Neurochemistry (Oxford). 23(3):457-464, 1974.

It is shown, using aminooxyacetate as metabolic inhibitor, that the process of oxidation of endogenous glutamate in incubated rat brain cortex slices follows a different course from that of exogenous L-glutamate. Endogenous glutamate is largely oxidized by an initial reaction with glutamate dehydrogenase with release of ammonia, but exogenous L-glutamate undergoes initial transamination to aspartate and alpha-oxoglutarate before oxidation occurs. In the presence of 2.5ml L-glutamate, it is found that, of the total exogenous glutamate utilized, 49% is converted to aspartate, 37% is converted to glutamine and the rest is fully oxidized through glutamate dehydrogenase. It is suggested that endogenous glutamate is normally oxidized in the neurons, and that glutamate released from neurons during excitation, and acting as exogenous glutamate, is taken up by the glia where it largely undergoes initial transamination before oxidation takes place. 35 references. (Author abstract)

196804 Saavedra, J. M.; Coyle, J. T.; Axelrod, J. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD 20014 **Developmental characteristics of phenylethanolamine and octopamine in the rat brain.** Journal of Neurochemistry (Oxford). 23(3):511-515, 1974.

Developmental characteristics of phenylethanolamine and octopamine in the rat brain were studied. Both substances show maximum concentration early, at 16 to 17 days of gestation. At this stage, the brain concentration of these amines is higher than that of norepinephrine. There is a sharp decline in the phenylethanolamine and octopamine concentrations on day 18 of gestation to approximately those of the adult. This decrease coincides with an increase in monoamine oxidase activity of fetal brain, with an increase in the activities of tyrosine hydroxylase and dopamine beta hydroxylase, and with the appearance of a saturable active uptake mechanism for norepinephrine. Effects of the amines on pregnant rats are discussed, and the possible significance of the findings in relation to pathological conditions such as phenylketonuria is considered. 24 references. (Author abstract modified)

196805 Hunt, W. A.; Majchrowicz, E. Neurobiology Dept., Armed Forces Radiobiology Research Inst. Defense Nuclear Agency, Bethesda, MD 20014 **Alterations in the turnover of brain norepinephrine and dopamine in alcohol-dependent rats.** Journal of Neurochemistry (Oxford). 23(3):549-552, 1974.

The turnover of brain norepinephrine (NE) and dopamine (DA) was studied in five groups of male Sprague Dawley rats under different conditions of alcohol treatment: no treatment, acute treatment while intoxicated, acute treatment subsequent to elimination of alcohol from the blood, alcohol dependence while still intoxicated, and alcohol dependence during a withdrawal syndrome. Turnover was determined from the rate of depletion of brain catecholamine levels after inhibition of tyrosine hydroxylase. In rats given a single dose of alcohol, NE turnover was increased, while DA turnover was unaffected during the first few hours after treatment. After that time the turnover of both NE and DA was reduced. In alcohol dependent rats, whether intoxicated or undergoing a withdrawal syndrome, the turnover of NE was increased, while that of DA was increased. Data suggest that catecholamines may mediate some of the symptoms of the alcohol withdrawal syndrome in the rat. 15 references. (Author abstract)

196808 Nahorski, S. R.; Rogers, K. J. Section of Pharmacology, Academic Division of Medicine, The University, Sheffield S10 2TN, England **The incorporation of glucose into brain glycogen and the activities of cerebral glycogen phosphorylase and synthetase: some effects of amphetamine.** Journal of Neurochemistry (Oxford). 23(3):579-587, 1974.

The effects of amphetamine sulphate on the incorporation of radioactive carbon from (U-14C) glucose into the glycogen of mouse cerebral cortex, midbrain and hindbrain were examined. In all brain regions studied, the amphetamine induced a rapid decrease in glycogen followed by a slower return to control values. No significant alterations were observed in the steady state concentration of cerebral glucose. Studies of the relative forms of the enzymes glycogen phosphorylase and glycogen synthetase suggest that rapid postmortem changes were less likely to occur if cerebral tissue were fixed by means of a freeze blowing technique. It is suggested that cerebral glycogen metabolism is controlled, at least in part, by the interconversion of the active and inactive forms of glycogen phosphorylase and synthetase. 36 references. (Author abstract modified)

197124 Carenzi, A.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Adenylcyclase in rat striatum and N. accumbens: stimulation by dopamine receptor agonists. (Unpublished paper).** Washington, D.C., NIMH, 1974. 1 p.

The effects of stimulation by dopamine receptor agonists on adenylcyclase in rat striatum and N. accumbens are reported. Rats were killed in 2 seconds and the concentrations of cyclic adenosine monophosphate (cAMP) in striatum, N. accumbens, pituitary and cerebellum were measured after ip injection of (+) amphetamine. cAMP was increased only in striatum and N. accumbens between 10 min and 30 min after injection. A similar increase was obtained with apomorphine. Pretreatment with 6-hydroxydopamine (6-OHDA) intraventricularly associated with reserpine decreased the adenylate cyclase activity of striatal homogenates. In the homogenates, dopamine or (+) amphetamine stimulated the adenylate cyclase activity; (+) amphetamine did not increase the adenylate cyclase activity of striatal homogenates from normal rats. Injection of (+) amphetamine increased the cAMP concentration of striatum in rats pretreated with 6-OHDA iv and reserpine ip. The action of (+) amphetamine is discussed in relation to the potent central nervous system stimulation elicited by (+) amphetamine given after 6-OHDA and reserpine injections. (Author abstract modified)

197211 Tsuru, Noriko; Asakura, Tetsuhiko. Dept. of Neuropsychiatry, Kagoshima Univ. School of Medicine, Kagoshima, Japan **Experimental studies on facilitative and inhibitory factors for epileptogenic focus formation.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(2):117-129, 1974.

The facilitative and inhibitory factors for secondary epileptogenic focus formation was studied in rabbits treated with eserin, atropine, safrazine and chlorpromazine. The time lag between the primary focus formation and the secondary mirror focus formation on the homologous area of the contralateral hemisphere is noted for each drug tested group and for a control group. In the atropine treated animals, the seizure discharge was easily propagated to the contralateral hemisphere and the time required to develop the secondary epileptogenic focus formation was the shortest. Spike discharges were inhibited by the arousal response induced by afferent stimuli in the control group and the groups treated with atropine and chlorpromazine. Seizure discharges were induced by afferent stimuli in the groups treated with eserine and safrazine. It is concluded that content of monoamine and acetylcholine in the brain plays an important part in epileptic phenomena. It is hypothesized that seizure is triggered by a breakdown in the equilibrium between the excitatory mechanism of the cortex and subcortex and an inhibitory mechanism is also mentioned. 16 references. (Author abstract modified)

197213 Ekstrom-Jodal, Barbro; von Essen, Claes; Haggendal, Egil; Roos, Bjorn-Erik. Dept. of Neurosurgery, Univ. of Goteberg, Sweden **Effects of L-DOPA and L-tryptophan on the cerebral blood flow in the dog.** Acta Neurologica Scandinavica (Kobenhavn). 50(1):3-10, 1974.

The effect of L-DOPA and L-tryptophan on the cerebral blood flow was studied in anesthetized dogs injected intravenously with one or other of the drugs. Cerebral blood flow was measured with the radioactive gas elimination technique with external gamma registration After L-DOPA there were signs of an increase of the cerebral blood flow followed later by a decrease. The effect of L-tryptophan on the cerebral blood flow in all experiments was a decrease. 26 references. (Author abstract)

197214 Ekstrom-Jodal, Barbro; von Essen, Claes; Haggendal, Egil. Dept. of Clinical Physiology, Sahlgren Hospital, S-413 45 Goteborg, Sweden **Effects of noradrenaline on the cerebral blood flow in the dog.** Acta Neurologica Scandinavica (Kobenhavn). 50(1):11-26, 1974.

The cerebrovascular response to intravenous noradrenaline infusion was studied in anesthetized dogs during different and carefully controlled blood gas and arterial blood pressure conditions, using the radioactive gas elimination technique with external gamma registration A flow reduction was found both at normocapnia and hypercapnia. In arterial hypoxia, which had induced vasodilatation, a corresponding vasoconstriction was found. The response could be blocked by the alpha-adrenergic blocking agent phentolamine. Autoregulation of cerebral blood flow was found to function well during the influence of noradrenaline as well as after adrenergic alpha-receptor blocking by phentolamine. 34 references. (Author abstract)

197215 Ekstrom-Jodal, Barbro; von Essen, Claes; Haggendal, Egil; Roos, Bjorn-Erik. Dept. of Neurosurgery, Sahlgren Hospital, S-413 45 Goteborg, Sweden **Effects of 5-hydroxytryptamine on the cerebral blood flow in the dog.** Acta Neurologica Scandinavica (Kobenhavn). 50(1):27-38, 1974.

The cerebrovascular response to intravenously infused 5-hydroxytryptamine was studied in anesthetized dogs with the radioactive inert gas elimination technique with external gamma registration A strong vasoconstrictory effect was found, which could not be abolished by either methysergide or alpha blockade The autoregulatory ability was found to be preserved. Even during arterial hypoxia, which has led to vasodilatation, serotonin constricts the cerebral vessels. 24 references. (Author abstract)

197277 Barth, N. Phamakologische Institute der Universitat D-65 Mainz, Obere Zahlbacher Strasse 67, Germany **The effects of the tricyclic antidepressants desmethylimipramine, doxepin and iprindole on the isolated perfused rabbit heart.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 277(Supplement):2, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effects of the tricyclic antidepressants desmethylimipramine, doxepine and iprindole on the isolated perfused rabbit heart were reported. Desmethylimipramine (DMI), doxepine (DOX) and iprindole (IP) reduced ventricular tension by about 60%. Atrial tension was decreased after DMI but remained unaltered after DOX and IP. DMI, DOX and IP reduced ventricular rate. The postganglionic sympathetic nerves were stimulated (STIM) electrically with different frequencies at intervals of 180 sec before (control period) and 20 min after infusion of DMI, DOX and IP. No arrhythmias were caused by STIM in the control period, after IP or after DMI. (Author abstract modified)

197278 Bernst, S. F. Neurologische Klinik der Universitat, D-8700 Wurzburg, Josef-Schneider-Strasse 2, Germany **Effects of lithium on cyclic 3',5'-AMP metabolism in rat brain.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):4, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effects of lithium on cyclic 3',5'-AMP metabolism in rat brain were reported. The intravenous as well as the intraperitoneal injection of LiCl failed to change cAMP

levels in rat frontal brain. Only after feeding the rats with 2mmoles/kg of LiCl for 8 days was a slight decrease in the cAMP content noticeable. The urinary excretion of cAMP did not differ from the controls. LiCl showed neither an influence on the activity of the high km phosphodiesterase nor on the low km enzyme, but inhibited the adenyl cyclase activity in a dose dependent manner. Results suggest that the psychotropic effects of lithium are related to the decrease of cAMP content in brain by inhibition of brain adenyl cyclase activity. (Author abstract modified)

197280 Burger, A. Institut fur Pharmakologie und Toxilologie der Universitat, D-8700 Wurzberg, Koellokerstrasse 2, Germany **Effects of reserpine and prenylamine on the noradrenaline fluxes of isolated splenic nerve granules.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):9, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effects of reserpine and prenylamine on the noradrenaline (NA) fluxes of isolated splenic nerve granules were reported. Noradrenaline (NA) granules prepared from postganglionic sympathetic splenic nerve trunks of cattle, exchanged 85% of their endogenous NA during incubation with adenosine triphosphate - magnesium (ATP-Mg). Preincubation and subsequent incubation with reserpine or prenylamine did not influence the NA content of the granules, while inhibiting, to the same extent, both influx and efflux. Under these conditions reserpine or prenylamine completely blocked the NA exchange. In the presence of NA, .01 micromoles of either drug did not influence the fluxes, whereas at NA this concentration of both drugs inhibited the fluxes by 30-40%. (Author abstract modified)

197282 Fernandes, M.; Hill, R.; Kluwe, S. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, D-1000 Berlin 19, Ulmenallee 30, Germany **The effect of chronic cannabis and cannabinoid application on the hepatic drug metabolizing system of the rat.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):16, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effect of chronic cannabis and cannabinoid application on the hepatic drug metabolizing system of the rat was reported. Cannabis and synthetic delta9-tetrahydrocannabinol (THC) were applicated for 9 months by means of drinking fluids to 40 male Wistar rats which were randomly assigned into four groups receiving the following treatments: tap water, vehicle, synthetic THC and cannabis extract. As compared to tap water animals no changes were found in the vehicle and the THC treated animals with respect to the microsomal content of protein, Cyt-P-450, Cyt b 5 and the activities of morphine demethylase, aminopyrine demethylase and aniline hydroxylase, respectively. In the cannabis group Cyt b 5 and Cyt-P-450 were slightly elevated. When the animals were killed immediately after stopping the treatment marked decreases in the activities of morphine and aminopyrine demethylases were to be found, probably due to cannabinoids present in the microsomal preparation. (Author abstract modified)

197283 Grossmann, W. Institute fur Pharmakologie, D-665 Homburg, Germany **Studies on the effect of amantadine on neuronal membranes.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):23, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the action of amantadine on the membranes of sensory nerve fibres was studied on dorsal root L6 or S1 isolated from rats. Action and resting potentials were determined by means of the sucrose-gap technique. Amantadine hydrochloride reduced the amplitude of the action potential without changing the resting potential. The membranes resistance was increased in comparison with the control. This effect is not significant on account of the small number of experiments. The repetitive activity was studied with long casting depolarizing pulses. The number and the amplitudes of subsequent action potentials were reduced after amantadine. The interval between two action potentials was shortened. In calcium free Loche solution no repetitive spike discharge was observed, which may be due to an asynchronous activity of each nerve fibre in the dorsal root. Amantadine added to the calcium free Loche solution elicited a repetitive discharge of spike potentials. (Author abstract modified)

197287 Lichtensteiger, W.; Lienheart, Ruth. Pharmakologisches Institut der Universitat, Gloriastrasse 32, CH-8006 Zurich, Switzerland **Effects of morphine, cholinergic agents and cold exposure on mid-brain dopamine (DA) nerve cells of morphine-tolerant and non-tolerant mice.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):43, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effects of morphine, cholinergic agents and cold exposure on midbrain dopamine (DA) nerve cells or of morphine tolerant and nontolerant mice were reported. During tolerance development the fluorescence intensity of DA neurons in the substantia nigra of mice did not change, but the intensity response to a single dose of morphine disappeared. DA nerve cells also exhibited a typical biphasic response of their fluorescence intensity to physostigmine which resembled the one induced in tuberal DA neurons by transsynaptic stimulation. In early morphine tolerance, this response was not completely suppressed but showed a clearly protracted course. This indicates that an input to the DA neurons resulting from cholinergic activity might change during the development of tolerance. Experiments with atropine and nicotine did not provide unequivocal information. Nicotine in a relatively high dose induced a rapid increase in fluorescence intensity. (Author abstract modified)

197288 Meyer, D. K.; Hertting, G. Pharmakologisches Institut der Universitat Wein, A-1090 Wien, Wahringerstrasse 13a, Austria **Influence of catecholamine uptake blocking drugs on the increase in water intake and plasma renin concentration induced by some hypotensive drugs.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):46, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the influence of catecholamine uptake blocking drugs on the increase in water intake and plasma renin concentration (PRC) induced by some hypotensive drugs were reported. Desmethylimipramine (DMI) increased the water intake induced by phentolamine (PH) significantly. The actions of isoproternol (IS) on both parameters remained unaffected by DMI. These results were confirmed by another uptake blocker study with amitryptiline. These results were confirmed by another uptake blocker study with amitryptiline. These results substantiate the hypothesis that the increase in PRC induced by hypotensive drugs is mediated by a stimulation of beta-receptors and that this rise in PRC causes the increase in water intake by releasing angiotensin which is known as a dipsogenic agent. (Author abstract modified)

197289 Pfeifer, A. K.; Csaki, L.; Komlos, M.; Schaefer, A. Institute of Experimental Medical Research, Hungarian Acade-

my of Sciences, Budapest, Hungary **The subcellular distribution of intraventricularly administered 3H-metaraminol in intact and rat brain pretreated with p-chloroamphetamine.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):54, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the influence of p-chloroamphetamine on the subcellular distribution of metaraminol (MA) was reported. Doses of 3H-MA were administered through a chronically implanted microcannule into the left ventricle and the rats were decapitated after one hour. P-chloroamphetamine was injected i.p. 2.5hours before the decapitation. In another series the rats received 50mg/kg alpha-methyl-m-tyrosine (MMT) i.p. simultaneously with 3H-MA. Results show that the subcellular distribution of MA is different when only 3H-MA was administered on one hand or when the rats were injected with MMT on the other hand. In the first case the amount of MA is considerably higher in the soluble fractions both in the primer and in the submitochondrial fractions than in the particulate fractions. In the second case significantly higher amounts of MA are accumulated in the particulate fractions and less in the soluble fractions. P-chloroamphetamine did not influence the subcellular distribution of MA. (Author abstract modified)

197290 Philippu, A.; Roensberg, W.; Przuntek, H. Institut Pharmkologie und Toxikologie der Universitat, D-8700 Wurzburg, Koellikerstrasse 2, Germany **Pressor responses to hypothalamic stimulation as influenced by drugs affecting adrenergic receptors.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):55, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, pressor responses to hypothalamic stimulation as influenced by drugs affecting adrenergic receptors were reported. Cats were anaesthetized with pentobarbital sodium and the hypothalamic posterior nucleus (HPN) superfused with artificial cerebrospinal fluid through a cannula. Superfusion of the HPN with piperoxan or tolazoline inhibited the pressor responses to electrical stimulation (ES) of the HPN. Labelling of the HPN with 3H-noradrenaline two hours before superfusion revealed that the inhibition of the pressor responses caused by tolazoline was accompanied by an increased release of the total radioactivity and an increased per cent release of 3H-noradrenaline. Superfusion with clonidine did not influence the pressor responses to ES of the HPN. Superfusion of the nucleus of the solitary tract (NST) with clonidine inhibited, while superfusion with tolazoline (1x10-1M) potentiated the pressor responses to ES of the HPN. It is concluded that alpha-adrenergic receptors are present in the HPN and are involved in the pressor responses evoked by ES, and in the regulation of the release of the neurotransmitter. (Author abstract modified)

197292 Rommelspacher, H.; Honecker, H. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, D-1000 Berlin 19, Ulmenallee, Germany **On the biotransformation of amphetamine in adult and old rats.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):63, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, using tritium labelled amphetamine the transformation of amphetamine to p-OH Amphetamine (p-OHA), p-OH Norephedrine (p-OHNe), conjugated p-OHA and hippuric acid was studied in the liver, cerebral cortex, brainstem, hypothalamus and plasma of adult and old rats. The time course was examined during 4 hours after injection. Differences between the two groups in half-times were only found for cortex, stem and hypothalamus. The turnover of amphetamine to p-OHA was slowed in the animals only in the brain, concerning the turnover of p-OHA to p-OHNE no age differences could be demonstrated. From 60 min, in the older group from 90 min a correlation was found between the decline of the hyperthermia and the concentration of amphetamine in plasma. During this period a certain concentration of amphetamine has a stronger effect on body temperature of adult rats than on that of the older group. (Author abstract modified)

197293 Schultz, J.; Daly, J. W. Institut Toxicologie der Universitat, D-7400 Tubingen, Wilhelmstrasse 56, Germany **Adenosine-3',5'-monophosphate in cerebral cortical slices from guinea pig and rat: effect of alpha- and beta-adrenergic compounds.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):70, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effect of alpha and beta adrenergic compounds on adenosine 3',5'-monophosphate in cerebral cortical slices from guinea pig and rat were reported. In cerebral cortical slices from guinea pig the formation of adenosine-3',5'-monophosphate (cyclic AMP) is not enhanced by the addition of norepinephrine or isoproterenol to the incubation medium. In rat, however, under the same conditions cyclic AMP levels are elevated 6-8 and 2-3 fold, respectively, over control levels. Adenosine stimulates formation of cyclic AMP in cerebral cortical slices from guinea pig and rat. In guinea pig, in the copresence of adenosine and norepinephrine a potentiation of the adenosine effect is observed (Sattin and Rall, 1970). This synergism can be blocked by the alpha-blocker phentolamine but not by the beta-blocker propranolol. In rat, a synergistic action is observed between norepinephrine and adenosine as well as between isoproterenol and adenosine. Use of phentolamine and propranolol as alpha-blocking and beta-blocking agents reveals the presence of alpha-receptors and beta-receptors in cerebral cortical slices from rat. It is concluded that in cerebral cortical slices from guinea pig the formation of cyclic AMP is stimulated via classical alpha-receptor. This receptor is sensitive to norepinephrine only in the presence of adenosine. (Author abstract modified)

197294 Stamm, T.; Wellman, W. Institut Pharmakologie, Medizinische Hochschule Hannover, 3000 Hannover-Kleefeld, Karl-Wiechert-Allee 9, Germany **Effects of catecholamines and prostaglandins on cyclic AMP levels in brain in vivo.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):74, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effects of catecholamines and prostaglandins on cyclic adenosine monophosphate (AMP) levels were examined in the in vivo brain. Microwave irradiation was used as method of sacrifice to estimate cyclic AMP levels in brains of rats and mice in vivo. Following intravenous injection of isoprenaline and dopamine, cyclic AMP levels in whole brains of mice were elevated by 70% and 40% respectively within one minute and had declined to control values after 3 minutes. Noradrenaline phenylephrine had no effect. The increase of cyclic AMP induced by isoprenaline was completely prevented by pretreatment with propranolol. This beta-receptor blocking agent had an effect of its own as a 30% decrease of cyclic AMP levels was observed 30 minutes after intraperitoneal injection. PGE1 and PGE2 led to a 60-70% increase of the cyclic AMP content, whereas PGF2 was much less effective. The estimation of cyclic AMP levels in seven discrete areas of rat brains showed that the increase of the cyclic nucleotide in response to PGE2 was highest in the cerebral cortex, inter-

mediate in the thalamus, and lowest in the cerebellum and brain stem. The cyclic AMP increase in brain was associated with opposite effects on the behavior of the animals, isoprenaline inducing central excitation and the E-prostaglandins inducing sedation. (Author abstract modified)

197295 Starke, K.; Montel, H.; Altmann, K. P. Pharmacologisches Institut, Gesamthoschule, D-4300 Essen, Huferandstrasse 55, Germany **On the inhibition of peripheral and central noradrenergic neurotransmission by clonidine.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):75, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effect of clonidine (C) on the release of noradrenaline (NA) in response to electrical stimulation of noradrenergic nerves was studied in isolated rabbit hearts (endogenous NA) and in slices of rat cerebral cortex (previously stored 3H-NA). At a stimulation frequency of 5 Hz, C diminished the stimulation induced overflow of NA. Complete inhibition could not be obtained: the concentration response curves levelled off at 68% and 35% inhibition in hearts and brain slices, respectively. The effect of C was inversely related to the overflow of NA under control conditions. Thus, the inhibition was reduced, if the control NA overflow was increased by raising the frequency of stimulation or by adding cocaine to the medium. In the presence of C, the increase of NA overflow caused by phenoxybenzamine or phentolamine, but not that caused by cocaine, was blocked. (Author abstract modified)

197296 Stock, R.; Krieglstein, J.; Rieger, H. Pharmakologisches Institut, Universitat D-6500 Mainz, Obere Zahlbacher Strasse 67, Germany **The effects of imipramine and promazine on energy metabolism and EEG of the isolated perfused rat brain.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 2R77(Supplement):77, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, imipramine and promazine were studied in regard to their effects on energy metabolism and the electroencephalogram (EEG) of the isolated perfused rat brain. During the perfusion, different EEG patterns were observed: modifications of the dominant frequency, spiking and a flat EEG with bursts of spikes (secondary discharges). The EEG modifications seemed to depend on drug concentration. In contrast to these effects on the EEG, the lower drug concentrations did not demonstrably affect cerebral metabolism. Only, when drug concentrations were raised to a toxic range, reflected in the EEG by the pattern of secondary discharges, higher levels of P-creatine and glucose and lower levels of glucose-6-P were detectable. The lactate/pyruvate ratio remained unchanged. No major differences in their effect on energy status and EEG were observed between imipramine and promazine, when equimolar drug concentrations were administered. (Author abstract modified)

197297 Theres, C. Institut fur Pharmakologie und Toxikologie Universitat des Saarlandes, 665 Homburg, Saar, Germany **The effect of two barbiturate antipodes on spinal reflexes and single motoneurons.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):80, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the stereospecificity of the effect of 1-methyl-5-phenyl-5-propyl-barbituric acid (+ or - MPPB) on monosynaptic and polysynaptic reflexes was studied in spinal rats. (+)-MPPB increased and (-)-MPPB reduced the amplitude of monosynaptic and polysynaptic reflexes. Both antipodes did not influence the amplitude and the conduction velocity of the early component of the afferent volley which was recorded from the dorsal roots. In cats, which were intercollicularly decerebrated and spinalized at the lower thoracic level, recordings were made from single motoneurones with microelectrodes. Both antipodes did not change significantly the amplitude of the action potentials elicited by antidromic stimulation. (+)-MPPB reduced the firing threshold to intracellular stimulation, whereas (-)-MPPB increased the threshold. (+)-MPPB increased and (-)-MPPB decreased monosynaptic and polysynaptic exitatory postsynaptic potentials produced by stimulation or dorsal roots or of the gastrocnemius nerves. The results indicate that the antipodes of MPPB exert an opposite effect on the motoneurone membrane. (Author abstract modified)

197298 Waldmeier, P. C.; Maitre, L.; Hedwall, P. R. Biological Research Laboratories, Pharmaceuticals Division, CIBA-GEIGY, Limited, Basel, Switzerland **Studies on alpha-methyldopa: relationship between metabolism, biogenic amines and antihypertensive effect.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):86, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, in renal hypertensive rats the cerebral contents of alpha-methyldopa, alpha-methyldopamine, alpha-methylnoradrenaline, dopamine and noradrenaline as well as blood pressure were determined simultaneously. The estimations of alpha-methyldopa and the amines were carried out by combining ion-exchange separation and differential fluorometric determination. The antihypertensive effect showed a time course closely associated with an increase in the content of cerebral alpha-methyldopamine and a decrease in dopamine, whereas lowering of blood pressure and changes in the levels of alpha-methylnoradrenaline and noradrenaline were dissociated. The results suggest that non-beta-hydroxylated catecholamines play a major role in mediating the antihypertensive effect of alpha-methyldopa. (Author abstract modified)

197299 Ahtee, L. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Catalepsy, stereotyped behaviour and striatal homovanillic acid content in rats treated with methadone.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 279(Supplement):23, 1973.

At the joint meeting of the British Pharmacological Society and the Deutschen Pharmakologischen Gesellschaft, the relationship between catalepsy, stereotyped behavior and striatal homovanillic acid (HVA) content was examined in rats treated with methadone. Acute administration of 10mg/kg of methadone produced maximum catalepsy but no stereotypies in control rats. In chronically treated rats 10mg/kg of methodone produced catalepsy the degree of which gradually decreased during the treatment. However, all these rats showed stereotyped behavior which appeared in about a week after starting methadone and was at its maximum after 5-6wks. Twelve hours after the last methodone injection the striatal HVA content in the rats treated for 8 weeks with methadone was 55% of that of the control rats. However, 2 h after the methadone injection the striatal HVA content was increased to about the same amount in both groups. These results suggest that the primary effect of methadone is catalepsy which causes increased dopamine production as a compensatory mechanism. (Author abstract modified)

197300 Scholtysik, G.; Salzmann, R. Biological and Medical Research Division, Sandoz Ltd., Basel, Switzerland **Interaction**

between antidepressant and centrally acting antihypertensive drugs. Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin) 279(Supplement):23, 1973.

At the joint meeting of the British Pharmacological Society and the Deutschen Pharmakologischen Gesellschaft, the interaction between antidepressant and centrally acting antihypertensive drugs was examined. Experiments were performed in conscious hypertensive rats using dibenzepine (DB) and desmethylimipramine (DMI) in combination with clonidine (C) and a clonidine like drug, BS 100-141 (BS). In DOCA hypertensive rats, DB did not significantly affect blood pressure itself but increased the antihypertensive effect. In Grollmann rats, DBI itself lowering blood pressure, increased effect of BS. DMI did not influence the antihypertensive effect of C. In order to see whether an interaction between DB and the antihypertensive drugs occurred within the CNS, studies were made on the effects of the drugs alone and in combination on noradrenaline (NA) turnover in rat brain stem. DB itself caused a small, but significant inhibition of NA turnover and markedly potentiated the inhibition induced by C and BS. The results suggest that the potentiation of the antihypertensive effects of C and BS produced by DB might be of central origin. (Author abstract modified)

197301 Kruk, Z. L. Department of Pharmacology and Therapeutics, London Hospital Medical College, Turner Street, London E1 2AD, England **Neurochemical bases for the anorectic activities of amphetamine and fenfluramine.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 279(Supplement):R24, 1973.

At the joint meeting of the British Pharmacological Society and the Deutschen Pharmakologischen Gesellschaft, the neurochemical bases of d-amphetamine (d-AM) and desethylfenfluramine (DEF) were studied in rats. The minimal doses of d-AM and DEF to decrease food ingestion by 90% in the first hour after presentation were 2.0mg/kg and 3.3mg/kg respectively. The dopamine (DA) receptor blocker pimozide (PZ), antagonized the action of d-AM but not of DEF. In contrast, the 5-hydroxytryptamine (5-HT) receptor blocker cyproheptadine (CPH), only antagonized DEF. Intracerebral injections of 10, 50 or 100 microg/rat of d-AM, DA, apomorphine, DEF or 5-HT, caused a dose dependent decrease in food intake. The results indicate that the anorectic actions of d-AM and DEF involve different central mechanisms; d-AM acts through dopaminergic receptors, DEF acts through tryptaminergic receptors. (Author abstract modified)

197302 Baker, S. P.; Hemsworth, B. A. Department of Pharmacy, University of Aston in Birmingham, Gosta Green, Birmingham 4, England **The effects of amphetamine and a related compound on MAO.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 279(Supplement):24, 1973.

At the joint meeting of the British Pharmacological Society and the Deutschen Pharmakologischen Gesellschaft, the effects of d-amphetamine and a related compound, 3,4-methylenedioxyamphetamine (MDA), on the MAO activity of different tissues both in vivo and in vitro was reported. d-amphetamine was found to be more potent than MDA as an inhibitor of MAO except when benzylamine was used as substrate with mouse and rat liver MAO. Pargyline was more potent than MDA and d-amphetamine on all enzyme preparations and with all substrates studied. Injections of d-amphetamine and MDA into mice produced little inhibition of mouse brain and liver MAO, whereas pargyline produced more than 90% inhibition. Differential centrifugation studies of brain and liver homogenates after i.p. injections show that amphetamine has little specificity for binding to the smae fraction as MAO; where amphetamine concentrations were high, MAO activity was low. These results suggest that inhibition of MAO plays a relatively small part, if any, in the CNS stimulating action of both MDA and d-amphetamine. (Author abstract modified)

197303 Turnbull, M. J.; McBride, A. Department of Pharmacology and Therapeutics, University of Dundee, Dundee, Scotland **The sensitivity of barbitone-dependent and withdrawn rats to tremorgenic drugs.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 279(Supplement).:25, 1973.

At the joint meeting of the British Pharmacological Society and the Deutschen Pharmakologischen Gesellschaft, the responsiveness of barbitone depdendent and withdrawn rats to three tremorgenic drugs physostigmine, oxotremorine and harmine were examined. Rats treated with barbitone sodium were more sensitive to oxotremorine and harmine. Four week treated rats showed a decreased sensitivity to physostigmine. Animals withdrawn after 4 weeks of barbiturate administration showed a rebound decrease in sensitivity to harmine (but not to oxotremorine) and an increase in sensitivity to physostigmine. The sensitivity to the tremorgenic drugs was not affected by a single injection of either barbitone sodium or pentobarbitone sodium, suggesting that the altered sensitivity described above was the result of prolonged exposure to or withdrawal from barbiturate. (Author abstract modified)

197304 Waterfield, Angela A.; Kosterlitz, H. W. Department of Pharmacology, University Medical Buildings, Foresterhill, Aberdeen, AB9 2ZD, Scotland **Acute 'tolerance, and 'dependence' in guinea-pig ileum.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 279(Supplement):26, 1973.

At the joint meeting of the British Pharmacological Society and the Deutschen Pharmakologischen Gesellschaft, the output of acetylcholine (ACh) and changes in the sensitivity of the smooth muscle to exogeneously applied ACh and histamine were examined. It was found that during acute morphine tolerance there was no recovey in ACh output but that there was an increase in sensitivity of the smooth muscle to acetylcholine and histamine. During acute dependence the level of ACh output remained low and the sensitivity of the smooth muscle to ACh and histamine returned to normal. If the twitch was restored to normal not by a large concentration of morphine but by naloxone, the output of ACh was also restored to normal. It is concluded that acute tolerance and acute dependence are postsynaptic phenomena whereas the specific action of morphine like drugs is on presynaptic sites. (Author abstract modified)

197305 Beckett, P. R.; Southgate, P. J.; Sugden, R. F. no address **The pharmacology of WY 23409, a new antidepressant.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 279(Supplement):R27, 1973.

At the joint meeting of the British Pharmacological Society and the Deutsche Pharmakologische Gesellschaft, the pharmacology of WY 23409, a new antidepressant, was reported. WY 23409 in mice reversed the hypothermic response to reserpine and in rats the same doses i.p. potentiated the weight loss caused by methamphetamine. Following the injection of WY 23409, imipramine or desipramine, the frequency response line of contractions of the cat nictitating membrane to nerve stimulation was displaced to the left in a parallel manner characteristic of potentiation. The same dose of each compound gave identical potentiation of the response to noradrenaline on blood pressure, but abolished the pressor response to

tyramine. WY 23409 and imipramine were equiactive in blocking the uptake of noradrenaline by rat cerebral cortex in vitro, but WY 23409 only inhibited the uptake of 5-hydroxytryptamine weakly and had only 1/10th the activity of imipramine in inhibiting monoamine oxidases. (Author abstract modified)

197445 Hancock, J. C.; Volle, R. L. Department of Pharmacology, Schools of Medicine and Dentistry, University of Connecticut, Hartford, CT 06112 **Responses of molluscan neurons to catecholamines.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):5-15, 1973.

The effects of norepinephrine, epinephrine and isoproterenol were studied on identified neurons in the visceral ganglion of Helix pomatia by standard microelectrode techniques. In five identifiable cell types, the catecholamines increased the rate of spontaneous firing. The excitatory action was accompanied by either no change in resting membrane potential (Em) or depolarization. In two other identifiable cell types, the catecholamines decreased the rate of spontaneous firing. The inhibitory effect was accompanied by no change in Em or hyperpolarization. Membrane resistance was not altered. The order of potency for either was: norepinephrine, epinephrine, isoproterenol in decreasing order. Dihydroergotamine blocked both the excitatory and inhibitory actions of the catecholamines. Propranolol and d-tubocurarine had no effect on either response. These data show that the actions of catecholamines on molluscan neurons differ markedly from those of central mammalian neurons. 10 references. (Author abstract)

197446 Pradhan, S. N.; Kamat, K. A. Department of Pharmacology, Howard University College of Medicine, Washington, DC **Effects of anticholinergic agents on self-stimulation.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):16-24, 1973.

The effects of several cholinergic antagonists were investigated on self-stimulation behavior in rats implanted with bipolar electrodes in two areas of their hypothalamus. As in the case of scopolamine reported earlier, other tertiary ammonium anticholinergic agents, such as atropine, JB 329 and JB 336 facilitated self-stimulation with either a constant or a stepping current in the majority of the rats. Scopolamine appeared to be most potent in this respect. The facilitatory effect of these drugs was usually marked at low baseline rates, although such effect was also observed in some rats at higher rates. As proposed earlier, self-stimulation responding appears to be dependent upon the balance between the activities of the adrenergic excitatory (go) and the cholinergic inhibitory (no go) systems. Anticholinergic agents enhance self-stimulation responding by blocking the cholinergic inhibitory system. 13 references. (Author abstract)

197447 Baltzer, V.; Bein, H. J. Biological Laboratories of the Pharmaceutical Division, Ciba-Geigy Limited, Basel, Switzerland **Pharmacological investigations with benzoctamine (Tacitin), a new psycho-active agent.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):25-41, 1973.

Benzoctamine, a new psychoactive compound with tranquilizing and muscle relaxant effects, was investigated in a variety of pharmacological experiments in animals. The results obtained clearly differentiate it from representatives of several groups of centrally active drugs. Benzoctamine does not produce signs of specific toxicity or teratogenicity. 17 references. (Author abstract modified)

197448 Gessner, P. K.; Gessner, T. Department of Pharmacology, State University of New York, Buffalo, NY **The interaction of barbital and testosterone relative to their hypnotic effects.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):52-58, 1973.

The interaction of barbital and testosterone were studied relative to their hypnotic effects. Testosterone administered i.p. in corn oil to mice causes righting reflex loss the ED 50 for which is 289.6mg/kg. Under similar conditions barbital has an ED 50 of 142.1mg/kg. Coadministered with barbital, testosterone can act synergistically in producing righting reflex loss. At high testosterone and low barbital doses the testosterone content of ED 50 mixtures is however not significantly different from the ED 50 for testosterone. In particular the ED 50 for a 2.8:1 molar testosterone - barbital mixture is significantly greater than would be expected on the basis of simple dose additivity. This phenomenon is seen to be associated with the much shorter onset of action of testosterone relative to the onset of action of barbital whereby upon administration of a testosterone rich mixture the effects observed are almost exclusively attributable to testosterone. 21 references. (Author abstract)

197449 Brus, R. Department of Pharmacology, School of Medicine, Zabrze 8, Poland **Effect of 6-hydroxydopamine on the level of the catecholamines in the brain of developing rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):71-76, 1973.

The effect of 6-hydroxydopamine (6-OHDA), administered i.p. in a dose of 200mg/kg, on noradrenaline (NA) and dopamine (DA) concentration in various parts of the brain of developing rats was examined. Twenty four hours after 6-OHDA injection, the decrease of NA in all examined parts of the brain of newborns and 7-day-old animals was observed. No changes were found in older animals. 6-OHDA did not affect DA levels in any parts of the brain in all examined age groups. The change in NA levels in young animals suggests that 6-OHDA crosses the blood-brain barrier only in the early stage of life. 24 references. (Author abstract)

197451 Riblet, L. A.; Mitchell, C. L. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52240 **The effects of cord section under ether or halothane on the ability of chlorpromazine to affect the jaw jerk response to tooth pulp stimulation in the encephale isole preparation.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):141-146, 1973.

The effects of cord section under ether or halothane on the ability of chlorpromazine to affect the jaw jerk response to tooth pulp stimulation in the encephale isole preparation were examined. Electrical stimulation of the tooth pulp with a single square wave pulse of 0.5msec duration or a train of 4 such pulses at 64 Hz was used to elicit the jaw jerk response in cats. In animals with intact spinal cords, chlorpromazine elevated the jaw jerk threshold after pretreatment with ether or halothane to a similar degree. In the encephale isole preparation, jaw jerk thresholds were also elevated when spinal section was done under ether anesthesia. In contrast, when spinal section was done under halothane anesthesia chlorpromazine did not elevate the jaw jerk thresholds. 8 references. (Author abstract modified)

197452 Davis, R. S.; McNeill, J. H. Tulane University School of Medicine, New Orleans, LA 70112 **The cardiac effects of cocaine and certain antihistamines and antidepressants.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(2):262-279, 1973.

The ability of cocaine and certain antihistamines and tricyclic antidepressants to stimulate cardiac force of contraction by releasing norepinephrine (NE) was tested. Chlorpheniramine, brompheniramine, tripelennamine, tripolidine, desipramine, imipramine, cocaine and tyramine were found to produce marked positive inotropic effects in isolated, spontaneously beating guinea pig right atria. Promethazine, however, depressed the force of contraction. Chlorpheniramine, tripelennamine, triprolidine, desipramine, cocaine and tyramine caused an increase in the efflux of H3-NE from isolated right atria perfused while in a tissue bath. This increase was associated with a positive inotropic effect for all drugs tested except desipramine. It is concluded that chlorpheniramine, tripelennamine, triprolidine and cocaine exert their positive inotropic effects via a tyramine like mechanism, that is by releasing NE from sympathetic nerve endings. It is suggested that desipramine, at doses which are not depressant to the atria, is acting primarily by blocking the uptake of spontaneously released NE. 33 references. (Author abstract modified)

197453 Babbini, M.; Torrielli, M. V.; Gaiardi, M.; Bartoletti, M.; De Marchi, F. Institute of General Pathology, University of Turin, Turin, Italy **Central pharmacological activities of 4-phenyl-6-chloro-1,4-dihydro-2H-3,1-benzoxazin-2-one.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(2):287-299, 1973.

Central pharmacological effects of 4-phenyl-6-chloro-1,4-dihydro-2H-3,1-benzoxazin-2-one (SAS-563) were investigated in mice and rats by various techniques. The central activity of the compound was mainly depressant in nature when compared with the antidepressant like action of the structurally related 2,3-dihydro-4H-1,3-benzoxazin-2-one-3-acetamide (F.I.6654). 15 references. (Author abstract)

197456 Baggot, J. D.; Davis, L. E.; Reuning, R. H. Massey University, Palmerston North, New Zealand **The disposition kinetics of amphetamine in the ruminant animal.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):17-27, 1973.

The disposition kinetics of amphetamine in goats, which have a digestive system peculiar to ruminant animals, was investigated. A very rapid distribution phase was followed by fast elimination of the drug which was probably due primarily to biotransformation. The extent of plasma protein binding, determined in vitro by equilibrium dialysis, was independent of drug concentration. A large apparent specific volume of distribution of the drug was observed. Analogue computer generated curves for the amount of drug in various compartments showed that the maximum concentration was present in tissues at 9 minutes and distribution was complete 10 minutes after the intravenous injection. It was concluded that a single compartment model is sufficiently accurate in describing the disposition kinetics of amphetamine. 40 references. (Author abstract modified)

197457 Hanig, J. P.; Seifter, J. Division of Drug Biology BD-413, FDA, Washington, DC 20204 **The effects of parenteral administration of catecholamines, serotonin and histamine on behavior and levels of these amines in the brain of the neonate chick.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):38-47, 1973.

The effects of parenteral administration of catecholamines, serotonin and histamine on behavior and levels of these amines in the brain of the neonate chick were examined. Epinephrine i.v. penetrated the blood-brain barrier (BBB) of the neonate chick, causing lethargy and an increase of 88% in its brain level. Endogenous dopamine was also significantly increased by 26%, suggesting endproduct repression of epinephrine biosynthesis. Parenteral serotonin penetrated the BBB and increased by 44% its brain level without significantly altering concentrations of other endogenous amines. Dopamine penetrated the barrier, caused catatonia and elevated its brain level by 144% without affecting brain levels of other amines. Lethargy and catatonia appear to be direct central effects of serotonin and dopamine respectively. Parenteral norepinephrine and histamine also caused lethargy but did not significantly alter brain levels of any of the amines measured including norepinephrine and histamine. 48 references. (Author abstract)

197458 Taska, R. J.; Schoolar, J. C. Texas Research Institute of Mental Sciences, Houston, TX 77025 **Peripheral tissue distribution, brain distribution and metabolism of mescaline-14C in monkeys.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):66-78, 1973.

The peripheral tissue distribution, brain distribution and metabolism of mescaline-14C in monkeys were studied. Mescaline crossed the blood-brain barrier in the monkey, but its passage across this barrier was limited by the high ionization (99.3%) of mescaline at physiological pH and by the low lipid solubility of the unionized form of mescaline. The relative distribution of radioactivity in the monkey brain showed little variation with time. The gray matter always contained a higher concentration of radioactivity than the white matter. Among the peripheral tissues, relatively high concentrations of radioactivity were found, prior to 2 hours, in the bone marrow, salivary glands, and adrenal and after 2 hours in the bile, kidney, liver, and lung. Through the first 6 hours less than 25% of the liver radioactivity consisted of mescaline metabolites. N-acetylmescaline was the major metabolite identified. 20 references. (Author abstract modified)

197460 Stepanek, J. Biological Research Laboratories, Ciba-Geigy, Ltd., Basel, Switzerland **Changes in acid-base balance, respiration rate and heart rate upon repeated oral administration of benzoctamine and diazepam to conscious dogs.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):135-152, 1973.

Changes in acid - base balance, respiration rate and heartrate upon repeated oral administration of benzoctamine and diazepam to conscious dogs were studied. After a dose of 3.0mg/kg of benzoctamine slight compensated metabolic acidosis and respiratory alkalosis were observed. A dose of 10mg/kg, gave rise to noncompensated respiratory and metabolic alkalosis which regressed within 24 hours of administration. Both doses slowed respiration. Only slight changes in PO2 and O2 saturation and in heartrate were noted. Diazepam, particularly at the higher dose level, led to metabolic acidosis, which became progressively more marked as medication continued; it was not compensated in the animals given 10mg/kg daily. Respiration was accelerated after a dose of 10mg/kg. O2 saturation was increased by each dose of diazepam administered, but the values recorded 24 hours after the last dose were distinctly lower than the pretreatment values. 22 references. (Author abstract)

197461 Caillard, C.; Rapin, J. R.; Bralet, J.; Rossignol, P. U.E.R. des Sciences Pharmaceutiques et Biologiques, 4 avenue de l'Observatoire, 75 Paris 6e, France /**Modification by desipramine of the adrenergic sensitivity of pyrogallol in the rat.**/ Modification par la desipramine chez le rat de la sensi-

bilisation adrenergique du pyrogallol. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):153-162, 1973.

The effect of pyrogallol, an inhibitor of catechol-O-methyltransferase (COMT), has been investigated on directly or indirectly elicited catecholamine pressor responses in pithed rat and on cardiac and plasma concentrations of tritiated norepinephrine and metabolites following norepinephrine-3H administration. The potentiation to exogenous and endogenous norepinephrine responses by pyrogallol was enhanced by desipramine. When the neuronal uptake of catecholamines was prevented by desipramine, pyrogallol was found to increase the cardiac levels of norepinephrine-3H. It was concluded that, if the uptake into sympathetic nerves is prevented, enzymatic degradation by COMT becomes more important in the inactivation of norepinephrine so that desipramine, which is a potent inhibitor of catecholamine uptake, will enhance the adrenergic potentiation by pyrogallol. 27 references. (Author abstract)

197463 De Moraes, S.; Do Carmo, M. Maria; Carvalho, F. V. Department of Pharmacology and Therapeutics, Faculty of Veterinary Medicine, University of Sao Paulo, Sao Paulo, Brazil **The effects of amphetamine and cocaine on the response of the isolated guinea-pig vas deferens to noradrenaline, tyramine and nerve stimulation.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):199-208, 1973.

The effects of amphetamine and cocaine on the response of the isolated guinea pig vas deferens to noradrenaline, tyramine and hypogastric nerve stimulation were studied. Tyramine and amphetamine increase the response to nerve stimulation whereas cocaine reduced the response. The effect of tyramine is antagonized by amphetamine and cocaine. In animals pretreated with reserpine and nialamide the response to hypogastric nerve stimulation was strongly reduced. Incubation with a high concentration of noradrenaline induced partial recovery of the response to nerve stimulation. Cocaine prevents the effects of noradrenaline while treatment of the preparation with amphetamine and noradrenaline caused a total recovery to nerve stimulation. Amphetamine and cocaine induced supersensitivity to noradrenaline but only cocaine increased the maximum response to the agonist. Amphetamine and cocaine shifted to the right the dose response curve to tyramine and reduced the maximal response to the indirectly acting amine. 30 references. (Author abstract modified)

197464 Bocknik, S. E.; Kulkarni, A. S. Department of Pharmacology, Research Center, Dow Chemical Company, Zionville, IN 46077 **Effects of anorectic agents on blood pressure of the dog.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(2):213-218, 1973.

Six anorectic compounds were examined for their blood pressure effects in the anesthetized dog. All drugs were administered intravenously through the femoral vein, while blood pressure was monitored via the femoral artery. The anorexiants -- aminorex and d-amphetamine, diethylpropion, fenfluramine, chlorphentermine, and phenmetrazine -- elicited an increase in blood pressure. All anorexiants significantly potentiated the tyramine pressor responses at all doses tested and had some effect on norepinephrine, with phenmetrazine and d-amphetamine significantly potentiating norepinephrine at all the doses examined. All compounds except fenfluramine had an effect on the isoproterenol decrease in blood pressure, but fenfluramine was the only anorexiant which enhanced the acetylcholine induced depressor effect. Minimal but significant effects on histamine were observed with some doses of aminorex, chlorphentermine and diethylpropion. 5 references. (Author abstract)

197465 Reiter, R. J.; Morgan, W. W.; Talbot, J. A. Department of Anatomy, University of Texas Medical School, San Antonio, TX 78284 **Seizures in rats induced by pinealectomy: influence of diazepam, chlordiazepoxide, and diphenylhydantoin and pineal substances.** Archives Internationales de pharmacodynamie et de Therapie (Ghent). 202(2):219-230, 1973.

The influences of diazepam, chlordiazepoxide, diphenylhydantoin and pineal substances on seizures in rats induced by pinealectomy were examined. When immature male rats are parathyroidectomized and a week later are pinealectomized, a large percentage of the animals exhibit seizures within the first 8 hr after pineal gland removal. In the present experiments, the post convulsive mortality (within 48 hr) of such rats was about 50%. The seizures are not a result of neural damage produced at the time of pinealectomy, but seem to be directly correlated with the loss of the pineal gland. The seizures are not altered by treatment of the animals with diphenylhudantoin but are inhibited, in a transitory manner, by a single injection of diazepam or chlordiazepoxide. Pentobarbital reduced the number of rats that convulsed in response to parathyroidectomy and pinealectomy. The administration of pineal substances (melatonin, beta-carboline or an aqueous bovine pineal extract) does not alter the convulsive behavior. 19 references. (Author abstract modified)

197466 Lipp, J. A. Defence Research Establishment, Suffield, Ralston, Alberta, Canada **Effect of benzodiazepine derivatives on soman-induced seizure activity and convulsions in the monkey.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(2):244-251, 1973.

The effect of clonazepam and nitrazepam upon soman induced seizure activity and convulsions was studied in the monkey. Intravenous administration of either of these drugs, after the onset of the activity, effectively terminated the convulsions and suppressed the seizure activity. Administration of diazepam, clonazepam or nitrazepam prior to exposure of soman prevented the onset of seizure activity and convulsions with clonazepam and nitrazepam having the longest effective duration. 15 references. (Author abstract)

197467 Hitzemann, R. J.; Loh, H. H.; Domino, E. F. Department of Pharmacology, University of California Medical Center, San Francisco, CA 94122 **Effect of phencyclidine on the accumulation of 14C-catecholamines formed from 14C-tyrosine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(2):252-258, 1973.

The effect of the psychotomimetic agent, phencyclidine, on the accumulation of 14C-cathecholamines formed from 14C-tyrosine administered intracerebrally to the mouse was studied. In doses from 3-30mg/kg phencyclidine was found to decrease the cerebral accumulation of 14C-dopamine and 14C-norepinephrine but to increase the accumulation of 14C-3-methoxytyramine and 14C-normetanephrine. The relevance of these findings to the psychosis induced by phencyclidine is discussed. 21 references. (Author abstract)

197468 Gaillard, J. M.; Friedli, P.; Tissot, R. Clinque Psychiatrique Universitaire de Geneve, Geneve, Switzerland **/Effects of the high doses of L-Dopa on electrical activity in the brain of the rabbit: interaction with the metabolism of 5-HT./** Effet de la L-Dopa a fortes doses sur l'activite electrique cerebrale du lapin (interaction avec le metabolisme de la 5-

HT). Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(2):342-352, 1973.

The effects of i.v. administration of high doses of L-Dopa with or without a decarboxylase inhibitor, are studied on the unanesthetized rabbit, in acute experiments. During the perfusion of L-Dopa alone a characteristic electric pattern appears, in which cortical desynchronization is associated with a slow synchronization of the rhinencephalon. This pattern is replaced, after the perfusion, by a prolonged waking state. In the animal pretreated with a decarboxylase inhibitor (Ro-4-4602) at low doses, the perfusion of L-Dopa provokes first a clear synchronization of the EEG activity, identical to the rabbit's slow wave sleep, and followed by a much more prolonged waking state than with L-Dopa alone. This initial synchronization of EEG is interpreted as due to a displacement of endogenous serotonin because of the transformation into dopamine of high quantities of L-Dopa entering the brain quickly, when the decarboxylase of capillaries is inhibited. 32 references. (Author abstract modified)

197469 Klinger, W.; Peiter, E.-M.; Schirrmeister, M.; Karge, E. Institut fur Pharmakologie und Toxikologie, Freidrich-Schiller-Universitat Jena, Germany **/The effect of beta-thiaminoketones on the aminopyrine-N-demethylation in vitro and in viva such as the hexobarbital sleeping time and L-ascorbic acid excretion in the rat./** Die Wirkung von beta-thiaminoketonen auf die amidopyrin-N-demethylierung in vitro und in vivo sowie auf die Hexobarbital-Seitenlagenzeit und L-Askorbinsaure-Ausscheidung bei der Ratte. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(1):16-22, 1973.

The effect of beta-thiaminoketones on the aminopyrine-N-demethylation and the hexobarbital sleeping time and L-ascorbic acid excretion in rats was studied. Four beta-thiaminoketones exerted a competitive, partly a noncompetitive inhibition of the amidopyrine-N-demethylation in 9000 g-liver supernatant of rats in dose dependence. Hexobarbital sleeping time was prolonged, when tested 1 hr after i.p. administration of the studied compounds. Amidopyrine-N-demethylation activity was lowered 3 hr after administration. After a three days treatment with these substances in different doses no significant influence on ascorbic acid excretion, hexobarbital sleeping time or amidopyrine-N-demethylation could be observed. The in vitro testing of inhibitory properties cannot be used as a hint to inducing activities. 10 references. (Author abstract)

197471 Lotti, V. J.; Torchiana, M. L.; Porter, C. C. Merck Institute for Therapeutic Research, West Point, PA **Investigations on the action and mechanism of action of diphenylhydantoin as an antagonist of tetrabenazine and reserpine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(1):107-116, 1973.

The action and mechanism of action of diphenylhydantoin as an antagonist of tetrabenazine and reserpine were studied. Diphenylhydantoin antagonizes the suppression of locomotion induced by tetrabenazine in mice and rats and the suppression of locomotion and hypothermia induced by reserpine in mice. This action of diphenylhydantoin does not appear to be common to anticonvulsant agents as a class, since twelve other anticonvulsant agents of various chemical classes were ineffective. The mechanism of action of diphenylhydantoin in this regard is yet unexplained, but appears to be different from that of known antagonists of tetrabenazine and reserpine since it does not share other pharmacological actions of these agents which are thought to be related to their mechanism of action as tetrabenazine or reserpine antagonists. 16 references. (Author abstract)

197472 Schayer, R. W.; Reilly, M. A. Rockland State Hospital, Research Center, Orangeburg, NY **Effect of psychoactive drugs on in vivo metabolism of 14C-histamine in mouse brain.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(1):123-129, 1973.

A number of psychoactive drugs have been tested for interaction with histamine metabolism in mouse brain by measuring their effects of (A) levels of 14C-histamine, 14C-methylhistamine and total 14C, 2 hr after intracerebral injection of 14C-histamine, and (B) levels of 14C-histamine and total 14C, 30 min after intracerebral injection of 14C-L-histidine. In test (A) monoamine oxidase inhibitors increased both 14C-methylhistadine and 14C-histamine. Imipramine reduced 14C-histamine. Possible mechanisms of action are discussed. In test (B) no active drugs were found. 16 references. (Author abstract)

197473 Pirch, J. H.; Osterholm, K. C.; Cohn, R. A.; Barratt, E. S. Department of Pharmacology and Toxicology, University of Texas, Galveston, TX 77550 **Studies on EEG tolerance to marijuana in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(2):213-220, 1973.

Electroencephalograph (EEG) tolerance to orally administered marihuana extract was studied in rats by measuring the integrated voltage of the electrocorticogram. Tolerance to marihuana induced decreases in EEG voltage was maintained when the dose was gradually raised from 20mg/kg to 100mg/kg delta9-tetrahydrocannabinol (THC). The dose response curve for the voltage decrease was shifted approximately eight fold to the right after 4 days of treatment with marihuana extract. When marihuana treatment was discontinued, a rebound increase in EEG voltage was observed. Tolerance also developed to the decrease in EEG voltage produced by 95% pure THC. These results provide neurophysiological evidence of functional tolerance to marihuana in the rat. 12 references. (Author abstract)

197474 Saelens, J. K.; Simke, J. P.; Allen, M. P.; Conroy, C. A. Research Department, Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ 07901 **Some of the dynamics of choline and acetylcholine metabolism in rat brain.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(2):305-312, 1973.

The dynamics of choline and acetylcholine (ACh) metabolism were examined in rat brain. When methyl-H3 choline is infused i.v. in rats, the specific activity of choline and acetylcholine increases curvilinearly in the cortex, midbrain and brainstem of rats. By assuming an open single compartment model, it is possible to determine the fractional rate constants and the rates of efflux of both choline and acetylcholine in these 3 brain areas. When rats are treated with 0.3mg/kg of physostigmine sulfate, there are no changes in the rate of ACh efflux despite statistically significant increases in the endogenous levels of acetylcholine in the midbrain and brainstem. 10 references. (Author abstract)

197475 Slater, P.; Stonier, P. D. Department of Physiology, University of Manchester, Manchester 13, England **EEG seizures produced by intraventricular quaternary ammonium compounds in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(2):335-341, 1973.

The quarternay ammonium compounds triethylcholine (TEC), hemicholinium-3 (HC-3) and tetraethylammonium (TEA), which have been shown previously to deplete brain acetylcholine (ACh) when injected into the cerebral ventricles of rats, were examined for their ability to cause cortical EEG seizures. Both TEC and TEA brought about prolonged seizure activity which was prevented by choline. Choline also prevents the depletion of brain ACh. It required a large dose of HC-3 to cause cortical EEG seizures although HC-3 is a potent inhibitor of ACh synthesis at low doses. Hexamethonium which blocked the EEG seizures produced by TEC and TEA, does not prevent the reduction in brain ACh. It appears unlikely that the EEG seizures are linked directly to the depletion of brain ACh. An action of the quaternary compounds at receptors which are blocked by hexamethonium could be responsible for the EEG effects. 8 references. (Author abstract)

197477 Rochus, L.; Sterckx, G.; Reuse, J. J. Laboratoire de Pharmacodynamie et de Therapeutique, Faculte de Medecine, Universite Libre de Bruxelles, Belgium **/The influence of chlorpromazine and reserpine on the metabolism of cerebral phospholipids in the rat in vivo./** Influence de la chlorpromazine et de la reserpine sur le metabolisme des phospholipides cerebraux chex le rat in vivo. Archives Internationale de Pharmacodynamie et de Therapie (Ghent). 203(2):407-410, 1973.

The effects of i.p. chlorpromazine or reserpine on the incorporation of 32P into different phospholipid fractions of rat brain were studied. Incorporation from 32P was decreased in all fractions by chlorpromazine and in some fractions only by reserpine pretreatment. Although chlorpromazine pretreatment caused an increased radioactivity level in blood plasma inorganic phosphate, brain inorganic phosphate level was the same after both drugs. 13 references. (Author abstract)

197478 Goldberg, M. E.; Sledge, K.; Dubinsky, B.; Robichaud, R. C. Department of Pharmacodynamics, Warner-Lambert Research Institute, Morris Plains, NJ 07950 **The influence of SKF-525A on the acute pharmacological properties of chlordiazepoxide.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(1):12-19, 1973.

Several properties of chlordiazepoxide were studied in rodents following inhibition of drug metabolizing enzyme systems with SKF-525A (2-diethylaminoethyl 2,2-diphenylvalerate hydrochloride). SKF-525A enhanced the antimaximal electroshock, antiaggressive and antianxiety effects of chlordiazepoxide. No important differences were observed after chlordiazepoxide in its inhibitory effects on avoidance behavior or its antipentetrazole and acute lethality effects in enzyme inhibited mice and rats. The results demonstrated that SKF-525A which presumably inhibited the metabolism of chlordiazepoxide resulting in higher concentrations of this agent at certain sites, did not uniformly alter its pharmacological and toxicological profile. 20 references. (Author abstract)

197479 Doggett, N. S. Department of Applied Pharmacology, Welsh School of Pharmacy, UWIST, King Edward VII Ave., Cardiff, Wales **Interaction of ouabain with pentobarbitone in the mouse.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(1):56-61, 1973.

The interaction of ouabain with pentobarbitone in the mouse was examined. Small doses of ouabain injected directly into the cerebral ventricles of the mouse markedly potentiate the hypnotic activity of pentobarbitone. In contrast, intraperitoneally administered ouabain in similar doses has no such effect. It is suggested that two mechanisms are involved in the observed potentiation: a direct interaction at the level of the central nervous system together with a minor indirect component resulting from a fall in body temperature. It is concluded that findings may be of clinical significance in cases of combined therapy with barbiturate hypnotics and the cardiac glycosides, when the hypnotic effect of the barbiturate may be significantly greater than anticipated. 12 references. (Author abstract)

197480 Fennessy, M. R.; Sawynok, J. Department of Pharmacology, University of Melbourne, Victoria 3052, Australia **The effect of benzodiazepines on the analgesic effect of morphine and sodium salicylate.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(1):77-85, 1973.

The effects of benzodiazepines on the analgesic effect of morphine and sodium salicylate were studied. Using the phenylquinone writhing method as a criterion for analgesia in mice, oral administration of chlordiazepoxide, clonazepam and flurazepam produced large analgesic ED50 values. No analgesic activity could be detected for diazepam, nitrazepam or medazepam up to 500mg/kg. Chlordiazepoxide enhanced morphine analgesia while the other benzodiazepines produced a significant reduction. Both chlordiazepoxide and clonazepam increased the analgesic activity of sodium salicylate, while nitrazepam reduced its activity. A complex picture was seen when the benzodiazepines were combined with sodium salicylate. Nitrazepam was the only compound not to prolong the analgesic activity of sodium salicylate. It is concluded that the benzodiazepines, although structurally similar, produce differing pharmacological effects when used in conjunction with analgesic agents. 13 references. (Author abstract modified)

197484 Ladefoged, O. Pharmacological Department, NOVO Terapeutisk Laboratorium A/S, NOVO Alle, 2880 Bagsvaerd, Denmark **The effects of LSD, psilocybin, harmaline and amphetamine on the body temperature of para-chlorophenylalanine pretreated rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(2):326-332, 1973.

The effects of four psychopharmacologically active compounds on the rectal temperature were examined in both untreated and para-chlorophenylalanine (pCPA) pretreated normal and febrile rats. The hyperthermic effect of amphetamine was reduced in both normal and febrile animals after pCPA pretreatment. Harmaline, psilocybin and LSD caused hypothermia in the rats. pCPA pretreatment antagonized the effect of harmaline but potentiated the effects of LSD and psilocybin. The same effect of pCPA pretreatment was seen in both the normal and the febrile animals. 15 references. (Author abstract)

197485 Stepanek, J. Biological Research Laboratories, Pharmaceutical Division, Ciba-Geigy Ltd., Basel, Switzerland **Alterations in acid-base balance in the dog after intravenous administration of benzoctamine and diazepam, compared with those induced by thiopental.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(2):350-360, 1973.

Alterations in acid - base balance in the dog after intravenous administration of benzoctamine and diazepam, were compared with those induced by thiopental. Benzoctamine, diazepam or thiopental sodium were given i.v. to dogs anesthetized with chloralose after their O2 saturation had reverted to normal. Benzoctamine exerted a stimulant effect on respiration, especially when given in a dose of 10mg/kg. The acid - base balance values remained within normal limits. Both doses of diazepam gave rise to respiratory acidosis, accompanied with a reduction in respiratory minute volume and

02 partial pressure. Hypoventilation was also demonstrable after the injection of thiopental in both doses, but was less marked and shorter lasting than that provoked by diazepam. 10 references. (Author abstract modified)

197486 Schaefer, J. F., Jr.; Loetzer, R.; Sofia, R. D. Department of Pharmacology, Wallace Laboratories, Cranbury, NJ 08512 **Effect of delta1-tetrahydrocannabinol and propranolol on ouabain induced arrhythmias.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 205(1):5-10, 1973.

The effects of propranolol and delta1-tetrahydrocannabinol (THC) on ouabain induced cardiac arrhythmias was investigated in pentobarbital anesthetized dogs. THC produced a transient hypotensive response of short duration. Propranolol produced a significant hypotensive effect for approximately 10 minutes. Both compounds delayed the onset of ventricular ectopic extrasystoles. While propranolol delayed the onset of the initial events of ouabain intoxication, THC did not. 4 references. (Author abstract)

197488 Jaeger, R. J.; Murphy, S. D. Department of Physiology, Harvard University School of Public Health, 665 Huntington Avenue, Boston, MA 02115 **Alterations of barbiturate action following 1,1-dichloroethylene, corticosterone, or acrolein.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 205(2):281-392, 1973.

The compounds 1,1-dichloroethylene, corticosterone and acrolein were tested for their effects on pentobarbital or hexobarbital sleeping time. 1,1-Dichloroethylene prolonged pentobarbital sleeping time between 2 and 4 hr after oral administration. Liver injury as measured by glucose-6-phosphatase depression was not detected at this time, and hexobarbital sleeping time was not affected. Corticosterone also prolonged pentobarbital sleeping time only. Acrolein prolonged both pentobarbital and hexobarbital sleeping time. The mechanism of these effects appeared to differ. 1,1-Dichloroethylene caused an altered absorption or distribution of pentobarbital. Corticosterone pretreatment resulted in an increase in the CNS sensitivity to pentobarbital. Acrolein produced ascites and increased hematocrit which may have altered the absorption or distribution of both barbiturates. The data suggest that the action of pentobarbital was more easily altered by changes in absorption, distribution or increased CNS sensitivity than was the action of hexobarbital. 14 references. (Author abstract)

197489 Sadovsky, E.; Weinstein, D.; Pfeifer, Y.; Polishuk, W. Z.; Sulman, F. G. Department of Obstetrics and Gynecology, Rothschild-Hadassah University Hospital, Jerusalem, Israel **Prevention of serotonin abortion by serotonin antagonists in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 205(2):305-316, 1973.

The prevention of serotonin abortion by serotonin antagonists in rats was examined. Abortion was induced in rats by intraamniotic injection of 0.02-0.1mg of the monoamine oxidase (MAO) blocker pargyline. This treatment engendered a rise in intrauterine serotonin and abortion in 87% of the fetuses. Treatment with four antiserotonin drugs: metergoline, dimetiotazine, NBMT, and pizotifen, which were injected subcutaneously 2-4 hours prior to the intraamniotic injection of the MAO blocker, allowed fetal salvage of 51% with metergoline, 54% with dimetiotazine, 36% with NBMT and 51% with pizotifen. The mechanism of fetal salvage is based on receptor competition between serotonin and the antiserotonin compounds. 24 references. (Author abstract)

197491 Takasaki, K.; Nishizawa, T.; Igisu, T.; Kaneko, M. Department of Pharmacology, Daiichi College of Pharmaceutical Sciences, Fukuoka, Japan **Relationship between the changes on blood pressure response and the cardiac catecholamine level after single and repeated administrations of tyramine and methamphetamine in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(1):150-160, 1973.

The relationship between the changes on blood pressure response and the cardiac catecholamine (CCA) level after single and repeated administrations of tyramine and methamphetamine in rats was examined. In anesthetized rats, the CCA level showed a maximal decrease 2 to 5 minutes after the intravenous administration of tyramine or methamphetamine. Tachyphylaxis with regard to blood pressure responses developed after three consecutive doses of methamphetamine, given at 5 minute intervals, but not after tyramine. At this stage the CCA level was normal after methamphetamine but lower than normal after tyramine. CCA was further diminished, up to a complete tachyphylaxis, by successive doses of tyramine. It is suggested that the mechanism of the development of tachyphylaxis may be mainly due to the accumulation of the drugs in the adrenergic nerve terminal. 25 references. (Author abstract modified)

197492 Schallek, W.; Kovacs, J.; Kuehn, A.; Thomas, J. Pharmacology Department, Research Division, Hoffman-La Roche, Inc., Nutley, NJ 07110 **Studies on clonazepam, flunitrazepam, and related benzodiazepines in cat and monkey.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(1):161-180, 1973.

The effects of benzodiazepines on behavioral and sleep tests in freely moving cats, and on tests for sedative and hypnotic activity in squirrel monkeys were examined. Ro 5-3027 was more potent than clonazepam and flunitrazepam in behavioral tests in cats. These benzodiazepines increased responding to both rewarded and nonrewarded signals; this effect was not shown by pentobarbital. Ro 5-3027 was more potent than clonazepam and flunitrazepam in sleep studies in cats. The benzodiazepines increased waking time on day 1 of administration, whereas sleeping time was increased on days 2 to 5. The initial increase in waking time was not seen with pentobarbital. Flunitrazepam was more potent than Ro 5-3027, clonazepam, or flurazepam hydrochloride in producing sedation in squirrel monkeys. The electrical activity of the brain showed high frequency patterns with little change in amplitude. Pentobarbital produced deep sleep; the electrical activity showed low frequency, high amplitude patterns. 8 references. (Author abstract)

197493 Kaul, P. N.; Farmer, M.; Grunder, J. R. 625 Elm Avenue, Norman, OK 73069 **Pharmacologic studies on propynyl dibenzazepine, a new alpha adrenergic blocker.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):229-241, 1973.

A new compound, 6-(2-propynyl)-6,7-dihydro-5H-dibenz (c,e)azepine (PDA), was found to be an alpha adrenergic blocker on isolated mouse vas deferens, guinea pig aortic strip and rat hind quarter vasculature, and a strong hypotensive in anesthetized as well as conscious dogs. Experiments conducted to study the mechanism of hypotensive action of PDA revealed that it acts by blocking the alpha adrenergic receptors at the sympathetic neuroeffector sites. 17 references. (Author abstract)

197494 Kaul, P. N.; Pabrai, P. R.; Farmer, M. 625 Elm Avenue, Norman, OK 73069 **Chlorpromazine metabolism VI –**

adrenolytic and antiserotonergic activities of chlorpromazine and its various metabolites. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):325-337, 1973.

The antiadrenergic and antiserotonergic activities of chlorpromazine and 11 of its metabolites were evaluated on the isolated in vitro systems as well as in the anesthetized rat. The comparative data obtained suggest that some metabolites, particularly the 7-hydroxy derivative of chlorpromazine, may also contribute toward the overall pharmacologic activity profile of chlorpromazine. The hydroxy metabolite appeared to be a stronger antiserotonergic compound than the parent drug in the in vitro test systems. 22 references. (Author abstract)

197495 de Moraes, S.; Bussato, P. A.; Carvalho, F. V. Laboratory of Therapeutics, Faculty of Veterinary Medicine, University of Sao Paulo, Sao Paulo, Brazil **A comparison of the effects of (+)-amphetamine, cocaine and denervation on the responses of the isolated vas deferens of the guinea-pig to norepinephrine and acetylcholine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):352-362, 1973.

A comparison of the effect of (+)-amphetamine, cocaine and denervation on the responses of the isolated vas deferens of the guinea pig to norepinephrine and acetylcholine is reported. During continuous exposure to (+)-amphetamine the dose response curves to norepinephrine in vasa deferentia removed from guinea pig not treated with reserpine were shifted to the left of the contralateral control curves and the sensitivity to acetylcholine was decreased. It is suggested that supersensitivity to norepinephrine induced by (+)-amphetamine is the result of the release of endogenous norepinephrine which distorts the dose response curves to exogenous norepinephrine. It is concluded that two components are responsible for the denervation supersensitivity: 1) the first component is related with the lack of drug specificity and moderate degree of increase in sensitivity; 2) the second component is responsible for the large increase in sensitivity to norepinephrine and results from the loss of the neuronal uptake of norepinephrine. 25 references. (Author abstract modified)

197496 Kafoe, W. F.; Leonard, B. E. Pharmacology Department, Organon, Scientific Development Group, Oss, the Netherlands **The effect of a new tetracyclic anti-depressant compound, Org GB94, on the turnover of dopamine, noradrenalin and serotonin in the rat brain.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):389-391, 1973.

The effect of a new tetracyclic antidepressant compound, Org GB94 on the turnover of catecholamines in the rat brain were examined. Org GB94 increased the turnover of noradrenaline, and to a lesser extent of dopamine, and has no apparent effect on the serotonin or catecholamine reuptake mechanisms. 11 references. (Author abstract)

197497 Rigter, H. Pharmacological Department, Organon Scientific Development Group, Oss, the Netherlands **Pharmacological influences on carbon dioxide-induced amnesia.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):397-398, 1973.

Pharmacological influences on carbon dioxide induced amensia were examined. CO2 induced amnesia could be attenuated by treatment with some ACTH analogs 1 hour before the retrieval trial. Administration of these analogs 1 hour before the acquisition trial was ineffective. The vasopressine analogue desglycinamide lysine vasopressine exerted an antiamnesic effect when injected before the retrieval trial as well as before the acquisition trial. (Author abstract)

197498 Van Delft, A. M. L.; Nyakas, C.; Kaplanski, J.; Tilders, F. J. H. Free University, Medical Faculty, Department of Pharmacology, Amsterdam, The Netherlands **The effect of 6-hydroxydopamine administration to neonatal rats on some endocrine and behavioral parameters.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):403-404, 1973.

The effects of 6-hydroxydopamine (6-OHDA) administration to neonatal rats on some endocrine and behavioral parameters were examined. Depletion of catecholamines in the rat brain as achieved by 6-OHDA treatment has minor effects on some parameters of endocrine or vegetative functions whereas a profound suppression of neocortical activation seems to be present. (Author abstract)

197566 Vizi, E. S.; Ronai, A. Z.; Knoll, J. Department of Pharmacology, Semmelweis University of Medicine, 1085 Budapest, Hungary **The inhibitory effect of dopamine on acetylcholine release.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):89, 1974.

At the 1974 Pharmacological Meeting at Graz, the inhibitory effect of dopamine on acetylcholine (ACh) release was reported. At 0.1Hz stimulation dopamine reduced the contraction of the isolated guinea pig longitudinal muscle strip without influencing the effect of exogenous ACh. Phentolamine prevented the effect of dopamine. The maximal effect of dopamine, however, could not be reached in the presence of phetolamine. In eserinized preparation dopamine reduced the release of ACh during resting condition and at low frequency of stimulation. In isolated basal ganglia of the rat dopamine reduced the release of ACh evoked by ouabain. Chlorpromazine enhanced the output of ACh during resting condition. It is concluded that dopamine where it plays any transmitter function (corpus striatum) might control the cholinergic transmission by inhibiting the release of ACh. The removal of dopaminergic control (6-OH-dopamine,chlorpromazine) enhanced the release and turnover of ACh. (Author abstract)

197567 Theisohn, M.; Friedrich, M.; Justus, P. Department of Pharmacology, Medical School, D-3000 Hannover, Karl-Wiechertallee 9, Germany **Heat production and oxygen consumption of the isolated rabbit heart under the influence of strophanthin verapamil, and glyceryl trinitrate.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):83, 1974.

At the 1974 Pharmacological Meeting at Graz, the energy consumption of the isolated, isovolumetrically beating rabbit heart was determined by the simultaneous measurement of O2 consumption. The effects of strophanthin, verapamil, and glyceryl trinitrate were studied under these conditions. Without drugs, the average heat production (H) and the O2 consumption (Q) were 1.405 cal/g dry wt min and 0.282 ml O2/g dry wt min over the whole range of volume variations. At a constant intraventricular volume strophanthin increased the developed pressure (DP). Verapamil decreased DP by 33% and H and Q by about 12%. GTN had no significant effect neither on the mechanical function nor on the parameters of energy consumption (H and Q). There was a significant parallelism between heat production and O2 consumption under all conditions tested. (Author abstract modified)

197568 Supek, Z.; Gjuris, V.; Tucan-Foretic, M. Department of Pharmacology, Medical Faculty, University, YU-41000 Zagreb, Salata 11, Germany **On the pharmacology of some beta-hydroxylated tryptamines.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 282(4):78, 1974.

At the 1974 Pharmacological Meeting at Graz, some pharmacological parameters of newly synthetized beta-hydroxytryptamines i.e. beta-hydroxytryptamine (I) and beta-hydroxyserotonin (II) were studied. Blood pressure, spontaneous respiration and resistance of the respiratory ways were recorded in guinea pigs under urethane anaesthesia. The spasmogenic activity was tested on isolated guinea pig ileum and rat stomach fundus strips. As reference substances serotonine and tryptamine were used. The effects of beta-hydroxylated tryptamines were fairly similar to that of their parent substances but there are some interesting differences worthwhile to be further studied. The effects of (II) on ileum and respiration are qualitatively similar to serotonin, but the beta-hydroxylated compound is approximately 6 times and 20 times, respectively, less active. Methysergic abolishes almost completely the effect of serotonin on the respiration, but scarcely the effect of (II). (Author abstract modified)

197569 Potkonjak, Dubravka. Department of Pharmacology, Medical Faculty, Sarajevo, M. Pijade 6, Yugoslavia **The relationship between rigidity and change in whole brain acetylcholine concentration produced by injection of reserpine in the rat.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):64, 1974.

At the 1974 Pharmacological Meeting at Graz, the relationship between rigidity and change in whole brain acetylcholine concentration produced by injection of reserpine in the rat was reported. Rigidity was induced by an intravenous injection of 7mg/kg of reserpine. It appeared 15 minutes after the injection and persisted for hours. The same dose of reserpine induced a significant increase in rat brain acetylcholine concentration which started 5 minutes after the injection and lasted two hours. Rigidity and brain acetylcholine were also estimated after intraperitoneal administration of either 10mg/kg of atropine sulphate or 1.5g/kg of gamma hydroxybutirate into rats previously pretreated with reserpine. Both drugs caused a significant decrease in reserpine induced rise in the rat brain acetylcholine. Atropine had no measurable effect on rigidity and gamma hydroxybutirate abolished it. The results indicate that reserpine produces rigidity mostly by monoaminergic inhibition. (Author abstract modified)

197570 Pik, K.; Borsy, J. Research Institute for Pharmaceutical Chemistry, 1325 Budapest, P.O.B. 82, Hungary **The mechanism of action of GYKI-32084, a new antiserotonin agent.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):B62, 1974.

At the 1974 Pharmacological meeting at Graz, the antiserotonin activity of N-methyl-9,10-dihydro-d-lysergic acid-nitroargininol (GYKI-32084) was investigated. The pA2 value of this compound is 9.80 on isolated rat uterus. It displays its activity in a competitive manner. The rat stomach fundus also contains D receptors; on this organ the effect however was noncompetitive. The pD2 value is 9.70. Atropine, guanethidine and morphine did not inhibit the serotonin reactions. (Author abstract modified)

197571 Magyar, K.; Knoll, J. Department of Pharmacology, Semmelweis University of Medicine, 1085 Budapest, Hungary Ulloi ut 26 **The effects of p-substituted amphetamines on the transmitter regulation in rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):53, 1974.

At the 1974 Pharmacological meeting at Graz, the effects of p-substituted amphetamines on the transmitter regulation in rat brain were reported. Among the p-substituted amphetamines studied, p-bromo-mehtamphetamine inhibited more selectively the uptake of 3H-serotonin (3H-5HT) on rat brain synaptosomal preparation. The inhibition of 5HT uptake was long-lasting and weeks were needed to reach complete recovery. The stereoisomers of V-111 were equipotent inhibitors of 5HT uptake while the (+)-isomer proved to be more potent inhibitor of 3H-noradrenaline (3H-NA) and 3H-dopamine (3H-DA) uptake. These results show that the more selective inhibition on 5HT uptake can be elicited by the (-)-isomer of the inhibitor. Experiments with 3H-V-111 showed that the substance itself intensively cumulate in the synaptosomal fraction. V-111 also induce some release of the transmitter amines, being the (+)-isomer more effective on NA and DA but not on 5HT release. (Author abstract modified)

197573 Lackovic, Z.; Jakupcevic, M. Institute Rudjer Boskovic, Zagreb, Salata 11, Yugoslavia **The action of psychostimulant sidnokarb on metabolism of biogenic amines in the brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):50, 1974.

At the 1974 Pharmacological meeting at Graz, the effect of psychostimulant sidnokarb (phenylcarbamyl derivative of 3-(beta-phenylisopropyl)-sydnone imine) on the metabolism of biogenic amines in the brain of rats was reported. After the application of this drug there are no changes in concentration of serotonin, noradrenaline and dopamine in the brain, but 5-hydroxyindoleacetic acid (5-HIAA), the main metabolite of serotonin, was significantly elevated. The turnover of serotonin, measured by accumulation of 5-HIAA in the brain after blockade of its transport to blood by probenecid, was significantly increased. (Author abstract modified)

197575 Kazic, T. Department of Pharmacology, Medical Faculty, Beograd-Yugoslavia **Catecholamine depleting action of physostigmine in the rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):R40, 1974.

At the 1974 Pharmacological meeting at Graz, pharmacological analysis of the norepinephrine (NE) depleting action of physostigmine was performed. This effect was found dose dependent over a narrow dose range. It was not affected during the tyrosine hydroxylase inhibition by AMT. Pretreatment with atropine, however, was found to prevent completely the action of physostigmine, while atropine itself significantly increased the endogenous NE content in the hypothalamus, but not in the brain stem. This points out that a muscarinic cholinergic mechanism regulates the endogenous NE levels in the brain. Beta adrenergic receptor blocking agent, propranolol was also found capable of preventing the NE depleting action of physostigmine. Alpha adrenergic receptor blocking agent, phenoxybenzamine was found itself to produce significant NE depleting action, thus precluding the possibility for a precise evaluation of the effect of physostigmine. (Author abstract modified)

197576 Hukovic, S.; Zvizdic, Elvedina; Erdeljan, D.; Radivojevic, M. Department of Pharmacology, Medical Faculty, Sarajevo, Yugoslavia **The inhibition of the effect of nerve stimulation by phenothiazines on isolated innervated organs.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):35, 1974.

At the 1974 Pharmacological meeting at Graz, the inhibition of the effect of nerve stimulation by phenothiazines on isolated innervated organs was reported. Five isolated organs

were oesophagus, urinary bladder, vas deferens, stomach and ileum prepared from three species: rats, mice and guinea-pigs. The nerves were cholinergic somatic, cholinergic vegetative and adrenergic, the muscle were smooth and striated. The phenothiazines were: chlorpormazine, thioridazine, trifluperazine and fluphenazine. The most effective inhibition of the stimulation was induced by phenothiazine on stomach and ileum. The less effective inhibition was induced on oesophagus and urinary bladder. The effect on vas deferens was chlorpromazine and the least was thioridazine. The inhibitory effect of Desmethylimipramine was the same as effect of chlorpromazine. (Author abstract modified)

197577 Ishida, Y.; da Ri, H.; Schmidt, G. Department of Pharmacology, University of Gottingen, D 34 Gottingen, Geistrasse 9, Germany **Effects of diazepam on discharge pattern in single fibres of phrenic nerve.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):35, 1974.

At the 1974 Pharmacological meeting at Graz, the effects of diazepam on spike interval, number of single discharges and respiratory rate were investigated in single, efferent phrenic nerve fibres of the anesthetized rat. Diazepam causes a dose dependent significant, continuous increase of the spike interval with simultaneous decrease of spike number for each inspiration. The respiratory rate was minimally elevated. These effects were demonstrated both on spontaneously breathing and artificially ventilated animals. No effect was elicited by an equal volume of solvent. The sensitivity to increase in chemical respiratory stimuli (hypercapnia, hypoxia) was unchanged by diazepam. It is suggested that the observed effects are not due to a direct action on the respiratory regulation systems and that an influence on the control of motor respiratory innervation should be considered. (Author abstract)

197579 Held, Katalin; Dallo, J.; Knoll, J. Department of Pharmacology, Semmelweis University of Medicine, 1085 Budapest, Ulloi ut 26 Hungary **Interaction between massed electroconvulsive shock and p-bromo-methylamphetamine (V-111) treatment.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):31, 1974.

At the 1974 Pharmacological meeting at Graz, the interaction between electroconvulsive shock (ECS) and p-bromo-methylamphetamine (V-111) treatment was reported. Ten consecutive shocks were given with 1 hour intervals. Five min after the last shock a complete inhibition of unconditioned escape reaction was observed. The depression was gradually eliminated and 12-24 hours after the last shock the CNS was in an excited state. Quick tolerance to massed ECS treatment developed if ECS was given on four consecutive days. Animals previously pretreated with V-111 for five consecutive days and given 10 ECS on the fifth day of treatment the acute depressive action of 10 ECS was eliminated. When 1, 3, 5, 10 ECS were given simultaneously with a three day V-111 treatment, tolerance did not develop to V-111 and massed ECS treatment. The complex interaction between ECS and V-111 which seems to attack selectively the 5-HT system needs further elucidation. (Author abstract modified)

197580 Fekete, M.; Herman, J.; Kelemenics, K. Institute for Experimental Medical Research, Hungarian Academy of Sciences, Budapest, Hungary **Measurement of serotonin turnover in rats with the help of monoamine oxidase inhibitors.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):R15, 1974.

At the 1974 Pharmacological meeting at Graz, the measurement of serotonin (5HT) turnover in rats with the help of monoamine oxidase inhibitors was reported. The increase of 5HT concentration in the brain of rats is biphasic in time after the injection of pargyline. The first rapid phase of increase takes place in the first 5 minutes after the injection of the enzyme inhibitor. Similar shape of the 5HT concentration curve was obtained employing other monoamine oxidase inhibitors. The rapid change of the 5HT level is highly dependent on the experimental circumstances (temperature, isolated or grouped animals). Assuming that the short time increase of the 5HT level is an indicator of the metabolic rate of this amine, the effect of ACTH was investigated in different brain regions. (Author abstract)

197581 Dakovic, K.; Banic, B.; Medakovic, M. Department of Pharmacology and Toxicology, Faculty of Medicine, Novi Sad, Hajduk Veljkova 7-9, Yugoslavia **The effects of some CNS-depressants on rats exposed to ionizing irradiation.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):11, 1974.

At the 1974 Pharmacological meeting at Graz, the effects of some central nervous system depressants on rats exposed to ionizing irradiation were reported. Rats of both sexes were conditioned in an automatic reflex conditioner to avoid in more then 80% of trials electric stimuli. The effects of drugs were changed in rats exposed to irradiation. Most prominent differences as compared to the controls were observed on the first and fourth day after the irradiation. Thus, 24 hour after irradiation the effects of chlorpromazine and hydroxizine were potentiated, whereas the effects of diazepam and Bayer 1470 were unchanged. Four days after irradiation the effect of chlorpromazine was potentiated, that of hydroxizine unchanged, and those of diazepam and Bayer 1470 partially inhibited. (Author abstract modified)

197582 Davila, D.; Davila, T. Department of Pharmacology, Medical Faculty, Zagreb, Yugoslavia **Effect of angiotensin II on serotonin accumulation in the rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):11, 1974.

At the 1974 Pharmacological meeting at Graz, the interaction of angiotensin II with brain serotonin (5-hydroxytryptamine, 5-HT) was analyzed. Rat brains were perfused through the ventricles with artificial cerebrospinal fluid containing 5-HT with or without angiotensin II. It was observed that 5-HT uptake was dose and time related. Angiotensin II reduced uptake of 5-HT in rat brain for about 40% or 60% respectively. Higher dose of angiotensin II did not cause additional reduction of uptake of labelled 5-HT. In the same time the content of 5-hydroxyindoleacetic acid roughly followed the pattern of 5-HT. Two angiotensin II analogs, namely, 8-alanin angiotensin II or 1-dimethylglycine, 8-isoleucine angiotensin II showed only minimal inhibition of 5-HT uptake. These analogs almost completely antagonized inhibitory effect of angiotensin II on 5-HT uptake. The later analog was more potent. These findings demonstrate that angiotensin II can also modulate uptake mechanism of 5-HT in the brain. (Author abstract modified)

197583 Carlsson, A.; Lindqvist, M.; Kehr, W. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg 33, Sweden **Postmortal accumulation of 3-methoxytyramine in brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):365-372, 1974.

The postmortal accumulation of 3-methoxytyramine in brain was examined in the rat. A rapid accumulation of 3-methoxytyramine occurred during the first hour after the decapitation of rats. The accumulation was enhanced by pargyline pretreat-

ment. It was less rapid at lower temperatures. The postmortal loss of dopamine corresponded to the formation of methoxytyramine in the pargyline treated rats but exceeded this formation in nontreated rats. Large amounts of methoxytyramine were also recovered from the basal ganglia of two human brains. 7 references. (Author abstract)

197584 Provoost, A. P.; Bohus, B.; de Jong, W. Rudolf Magnus Institute of Pharmacology, University of Utrecht, Medical Faculty, Vondellaan 6, Utrecht, the Netherlands **Neonatal chemical sympathectomy: functional control of denervation of the vascular system and tissue noradrenaline level in the rat after 6-hydroxydopamine.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):353-363, 1974.

In adult rats, the degree of vascular sympathectomy following neonatal administration of 6-hydroxydopamine (6-OHDA) was assessed. In treated rats, anaesthetized with pentobarbital, mean arterial blood pressure, heartrate and pressor response to tyramine were reduced, while pressor responses to noradrenaline, adrenaline, angiotensine II and arginine - vasopressin were markedly increased. The change of both the noradrenaline and tyramine response was also present in rats treated on days 1, 2 and 8, but absent in rats treated on days 1 and 2 only. Pressor responses to electrical stimulation of the sympathetic outflow of the spinal cord and of the posterior hypothalamus of treated rats were diminished and were practically absent after adrenalectomy. The 6-OHDA treatment caused gross depletion of noradrenaline (NA) from the spinal cord, and from peripheral organs and tissues except the adrenals. A reduced NA level in brain cortex was associated with an increase of that of the brain stem. 16 references. (Author abstract modified)

197585 Polc, P.; Mohler, H.; Haefely, W. Department of Experimental Medicine, F. Hoffmann-La Roche & Co., Ltd., CH-4002 Basel, Switzerland **The effect of diazepam on spinal cord activities: possible sites and mechanisms of action.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):319-337, 1974.

The effect of diazepam on several activities of the spinal cord was investigated in decerebrate and high spinal cats by recording neurograms from lumbosacral ventral and dorsal roots and by measuring the levels of gamma-aminobutyric acid (GABA) in the lumbosacral spinal cord. Diazepam depressed but did not abolish monosynaptic and polysynaptic ventral root reflex (VRR) responses. Dorsal root potentials (DRP's) and the presynaptic inhibition of monosynaptic VRR's elicited by stimulation of peripheral afferents were enhanced and prolonged by diazepam to the same extent in spinal and decerebrate animals. Thiosemicarbazide, which decreased the level of GABA in the spinal cord by about 60%, reduced presynaptic inhibition and DRP's and prevented the augmenting effect of diazepam on these parameters. It is concluded that diazepam affects various activities of the spinal cord predominantly by a spinal site of action, normal levels of GABA in the spinal cord seem to be a prerequisite for the augmenting effect of diazepam on presynaptic inhibition in the spinal cord, and diazepam may act by altering the metabolism or disposition of GABA. 31 references. (Author abstract modified)

197682 Gerardy, J.; Dresse, A. Laboratoire de Pharmacologie, Universite de Liege, 32, Boulevard de la Constitution, B-4000 Liege, Belgium /**Action of neuroleptics on the content of dopamine and DOPAC in the rat caudate nucleus.**/ Action des neuroleptiques sur le taux en dopamine et en DOPAC du noyau caude de rat. Experientia (Basel). 30(5):523-524, 1974.

The action of five neuroleptics and of a sedative drug on the content of dopamine (DA) and 3,4-dihydroxyphenylacetic acid (DOPAC) in the rat caudate nucleus has been investigated. The neuroleptics, haloperidol, pimozide, chlorpromazine, levomepromazine, increase the DOPAC amount significantly, while the DA remains unchanged. Reserpine significantly decreases DA but also weakly the DOPAC level. Promethazine has no effect upon the DA and DOPAC level. A seasonal variation of the DA content has also been observed. The duration of the neuroleptic action on DOPAC parallels self-stimulation behavior. A presynaptic action of these drugs may be implied in the DOPAC increase. 19 references. (Journal)

197742 Johnson, D. D.; Crichlow, E. C.; Crawford, R. D. Department of Medical Pharmacology, University of Saskatchewan Saskatoon, Saskatchewan S7N0W0, Canada **Epileptiform seizures in domestic fowl. IV. The effects of anticonvulsant drugs.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(5):991-994, 1974.

The ability of phenobarbital, diphenylhydantoin, trimethadione, and diazepam to modify epileptiform electroencephalogram (EEG) activity and prevent motor seizures in chickens genetically predisposed to convulsions was observed. These drugs prevented motor seizures and suppressed changes in the EEG normally induced by intermittent photic stimulation without producing an observable effect on the interictal EEG. 5 references. (Author abstract)

197744 Olesen, O. Vendelin; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus Univ. Psychiatric Institute, DK-8240 Risskov, Denmark **Effect of prolonged lithium ingestion on glucagon and parathyroid hormone responses in rats.** Acta Pharmacologica et Toxicologica (Copenhagen). 34(4):225-231, 1974.

The hypothesis that long-term lithium administration produces a general lowering of hormone responses that are mediated via the adenyl cyclase - cyclic adenosine 3',5'-monophosphate (AMP) systems in the rat was tested. Serum lithium concentrations were maintained at a level of 0.7to 0.9mM in rats. Lithium administration did not lower the response to parathyroid hormone as measured by the decrease in the urinary excretion of calcium and by an increase in urinary excretion of phosphate and cyclic-AMP; on the contrary, the effects of parathyroid hormone were higher in the lithium than in the control group. Lithium did not lower the response to glucagon as measured by liver glycogen breakdown. The liver glycogen concentration was equal in the lithium and in the control group before the hormone was administered; 1 hr after its administration the liver glycogen concentration was reduced by about 40% in both groups. Lithium led to an increase in the response to glucagon as measured by the increase in the urinary excretion of cyclic-AMP. The hypothesis was rejected. 14 references. (Author abstract modified)

197788 Sedlacek, Jindrich. Research Laboratory of Psychiatry, Charles University, 120 00 Prague, Czechoslovakia **Morphological, biochemical, and functional changes in chick embryonic brain tissue after intracerebral administration of ouabain.** Developmental Psychobiology. 6(6):567-577, 1973.

The manifestations of intracerebral administration of 3.4x 10-4M ouabain were studied in 15- and 19-day-old chick embryos. No significant changes in the histological structure of the cerebrum were detected in 15-day-old embyros. The (Na+-K+)-ATPase activity was completely suppressed, however, and the spontaneous bioelectric activity was inhibited. In 19-day-old embyros distinct swelling and vacuolization of the cel-

lular elements occurred. The (Na+-K+)-ATPase activity was inhibited to the same extent in 19-day-old as in 15-day-old cerebral tissue. Ouabain administration resulted in episodes of spike-and-wave paroxysmal activity in the EEG of 19-day-old embyros, characterized by high amplitude and low frequency discharges. Spontaneous motor activity was inhibited following an initial transient increase. In some cases short episodes of hyperactivity were registered, regularly followed by complete inactivity. 25 references. (Author abstract)

197811 Schulz, Rudiger; Cartwright, Christine. Department of Pharmacology, Stanford University, Medical Center, Stanford, CA 94305 **Effect of morphine on serotonin release from myenteric plexus of the guinea pig.** Journal of Pharmacology and Experimental Therapeutics. 190(3):420-430, 1974.

The uptake and release of exogenous 3H-5-hydroxytryptamine (5-HT) by the electrically stimulated longitudinal muscle - myenteric plexus preparation of the guinea pig ileum was measured. No significant difference in uptake was seen between normal and morphine tolerant strips. The preparation releases 5-HT spontaneously and electrical stimulation increases the efflux. The electrically induced release of radioactive neurotransmitter was blocked by tetrodotoxin but not by atropine. Morphine did not affect the release. Results support findings that the morphine tolerant guinea pig ileum is supersensitive to 5-HT. Morphine inhibited 5-HT induced twitches less effectively in tolerant preparations, and submaximal electrical stimulation applied to tolerant strips caused greater twitch tensions compared with normal strips. It is concluded that the action of morphine does not affect the presynaptic release of serotonin. The narcotic opiate could act postysnaptically. 29 references. (Author abstract)

197813 Korduba, C. A.; Veals, J.; Symchowicz, S. Department of Biochemistry, Schering Corporation, 86 Orange St., Bloomfield, NJ 07003 **Effects of 5-(n-butyl)-picolinamide (Sch 10595), a dopamine-beta-hydroxylase inhibitor, on serotonin and catecholamine metabolites in brain.** Journal of Pharmacology and Experimental Therapeutics. 190(3):459-465, 1974.

The effects of 5-(n-butyl)-picolinamide (Sch 10595), a dopamine-beta-hydroxylase inhibitor, on serotonin and catecholamine metabolites in brain were studied. Endogenous brain 5-hydroxyindoleacetic acid (5-HIAA) levels were markedly increased after mice received Sch 10595 05-(n-butyl)-picolinamide0, 100mg/kg; the maximum increase was detected at 3 hours. Endogenous brain 5-hydroxytryptamine levels were elevated significantly at 1 and 2 hours. There was also a dose related increase of 14C-5-HIAA formed from intracisternally injected 14C-5-hydroxytryptamine at 3 hours post-treatment. The increased levels of 5-HIAA after Sch 10595 treatment were not due to increased rate of 5-hydroxytryptamine synthesis or release. Sch 10595 was shown to impair efflux of 14C-5-HIAA from the mouse and rat brain, and the compound also elicited an increased level of acids in rat brain formed from intracisternally injected 14C-dopamine. This effect of Sch 10595 apparently does not relate to its dopamine-beta-hydroxylase inhibitory activity since two other dopamine-beta-hyrdoxylase inhibitors, U-14, 624 and disulfiram, did not impair the efflux of acidic metabolites of catecholamines from the brain. 19 references. (Author abstract)

197814 Bell, J. A.; Martin, W. R. NIDA Addiction Research Center, Leestown Pike, P.O. Box 2000, Lexington, KY 40507 **Studies of tryptamine and lysergic acid diethylamide (LSD) on cutaneous C-fiber and polysynaptic reflexes in the cat.** Journal of Pharmacology and Experimental Therapeutics. 190(3):492-500, 1974.

The effect of tryptamine and lysergic acid diethylamide (LSD) on cutaneous C fiber and polysynaptic reflexes in the cat were studied. The superficial peroneal nerve of the acute decerebrate spinal (L1) cat was stimulated with a voltage and duration maximal for C fiber activation. Short latency polysynaptic reflexes (PSR) and long latency C fiber reflexes (CFR) were recorded from an ipsilateral S1 ventral root. The facilitation by tryptamine was antagonized by cyproheptadine. Lysergic acid diethylamide (LSD) infused for 40 minutes produced facilitation of the CFR which reached a maximum of 297% of control 60 minutes postinfusion. Facilitation of the PSR by LSD was significant only immediately postinfusion. LSD produced no further increase in the CFR after facilitation produced by methysergide. It was demonstrated that tryptamine and LSD have a similar mode of action on spinal cord CFR, and that tryptamine and LSD produce a greater facilitation of the CFR than the short latency PSR. 29 references. (Author abstract modified)

197821 Goldstein, Dora B.; Kakihana, Ryoko. Department of Pharmacology, Stanford University School of Medicine, Stanford, CA 94305 **Alcohol withdrawal reactions and reserpine effects in inbred strains of mice.** Life Sciences (Oxford). 15(3):415-425, 1974.

Alcohol withdrawal reactions and reserpine effects in inbred strains of mice were examined. Mice of different inbred strains were treated with ethanol for 3 days, by inhalation of alcohol vapor and daily injections of pyrazole. Within strains, alcohol adapted mice were compared with controls. The alcohol adapted mice received 3.8% alcohol in their drinking water for one week and 7.5% alcohol for the next 16 or 19 weeks. During the inhalation period, C57BL mice had lower blood alochol levels than DBA mice, and alcohol adapted mice had slightly lower blood levels than controls. The withdrawal scores of C57BL mice were significantly lower than those of DBA, BALB or Swiss-Webster mice, more so than could be accounted for by the difference in blood alcohol levels. Mice of three strains were treated with reserpine and observed for behavioral effects, including convulsions on handling. Strain differences in reserpine effects closely paralleled the strain differences in alcohol withdrawal seizures. 19 references. (Author abstract)

197829 Candy, J. M.; Boakes, R. J.; Key, B. J.; Worton, Eve. MRC Neuropharmacology Unit, The Medical School, Birmingham B15 2TJ, England **Correlation of the release of amines and antagonists with their effects.** Neurpharmacology (Oxford). 13(6):423-430, 1974.

The microiontophoretic release of (14C)-noradrenaline into saline and rat brain tissue and the effect of a backing current of 15 nA on this release has been determined. It was found that the transport number of noradrenaline was similar for saline and tissue and that the backing current could markedly reduce the release of noradrenaline. The microiontophoretic release of (35S)-chlorpromazine has been studied. The release was linearly related to the charge passed for only two out of the ten micropipettes tested and the transport number of these was very low. An attempt has been made to determine the range of diffusion after microiontophoretic release of alpha-methylnoradrenaline and noradrenaline using the fluorescence method for the demonstration of biogenic monoamines and soluble compound autoradiography. The results show that these substances can diffuse for considerable distances and therefore possibly affect more than one neurone. There appears to be a correlation between the effects of perfusing a range of concentrations of noradrenaline on the electroen-

cephalic and the amount of noradrenaline that is taken up by the tissue. The amount of noradrenaline that diffuses into the tissue under the conditions that produce phasic arousal can be released microiontophoretically by a relatively low charge. 14 references. (Author abstract)

197832 Rump, S.; Grudzinska, E. Department of Toxicology, Military Institute of Hygiene and Epidemiology, Warsaw, Poland **Investigations of the effects of diazepam in acute experimental intoxication with fluostigmine.** Archives of Toxicology (Berlin). 31(3):223-232, 1974.

The therapeutic effectiveness of diazepam in organophosphate intoxication was studied in rats. It was demonstrated that this drug as an adjunct to a mixture of atropine and obidoxime raised the LD50 of fluostigmine in rats to a value about 80 times that in untreated rats. Diazepam alone had no therapeutic effect in these conditions. Diazepam quickly abolished the convulsive electrical activity of the rabbit cortex induced by fluostigmine, normalized the fluostigmine increased amplitude of indirectly elicited twitches of the skeletal muscle of the rat and arrested the disintegration of the muscle action potential observed in these cases. Diazepam had no influence on the block of tetany or on desynchronization of the basal bioelectrical activity of the cortex due to fluostigmine. 17 references. (Author abstract)

197858 Fernandes, Mario; Schabarek, Ahmed; Coper, Helmut; Hill, Regina. Institut fur Neuropsychcopharmakologie der Freien Universitat Berlin, D-1000 Berlin 19, Ulmenallee 30, Germany **Modification of delta9-THC-actions by cannabinol and cannabidiol in the rat.** Psychopharmacologia (Berlin). 38(4):329-338, 1974.

Cannabinol (CBN) and cannabidiol (CBD) were tested in several test procedures known to be altered by delta9-tetrahydrocannabinol (THC) or crude cannabis preparations. They were inactive in doses up to 8mg/kg in tests on animal motility, food and water intake, body temperature and catalepsy. In contrast, CBD enhanced the hexobarbitone sleeping time more pronounced than THC whereas CBN increased the sleeping time only slightly. When administered in combination CBD prolonged all actions of THC, whereas CBN selectively blocked the effect of THC on hexobarbitone sleeping time. The enhancement by CBD is best explained by an inhibition of THC metabolism. 21 references. (Author abstract)

197864 Gray, William D.; Rauh, Charles E. Schering Corp., P.O. Box 32, Lafayette, NJ 07848 **The anticonvulsant action of the carbonic anhydrase inhibitor methazolamide: possible involvement of a noradrenergic mechanism.** European Journal of Pharmacology (Amsterdam). 28(1):42-54, 1974.

The anticonvulsant action of the carbonic anhydrase inhibitor methazolamide was studied. The l-aromatic amino acid decarboxylase inhibitor Ro 4-4601/1 abolished the restorative action of d,l-dopa in reserpine and phenoxybenzamine treated mice without evidence of significant inhibiton of l-aromatic amino acid decarboxylase in brain. Depletion of extracerebral stores of norepinehrine by the i.v. administration of 6-hydroxydopamine abolished the anticonvulsant effect of methazolamide. The anticonvulsant action of the carbonic anhydrase inhibitor in 6-hydroxydopamine treated mice was restored by the administration of d,l-dopa. The antagonist action of the alpha blockers studied appeared to be specifically related to alphalpha-adrenergic blockade because potency and duration of antagonist action correspond with potency and duration of alpha-adrenergic blockade, phenoxybenzamine failed to antagonize the anticonvulsant action of diphenylhydantoin, the anticonvulsant action of methazolamide was not abolished when phenoxybenzamine was given after the carbonic anhydrase inhibitor, d,l-dopa administration reversed the antagonist action of phenozybenzamine, and the beta-hydroxylase inhibitor U-14624 annulled the reversal of phenoxybenzamine's antagonist action by d,l-dopa. 14 references. (Author abstract modified)

197868 Garattini, Silvio; Bareggi, Silvio R.; Marc, Viviana; Calderini, Gabriella; Morselli, Paolo L. Istituto di Ricerche Farmacologiche Mario Negri, Via Eritrea 62, 20157 Milan, Italy **Effects of piribedil on noradrenaline and MOPEG-SO4 levels in the rat brain.** European Journal of Pharmacology (Amsterdam). 28(1):214-216, 1974.

The effects of piribedil on noradrenaline and MOPEG-SO4 levels in the rat brain were studied. I.p. administration of piribedil methansulphonate to male Sprague-Dawley rats resulted in a remarkable increase of brain MOPEG-SO4 which was consistent over time. In parallel experiments brain content of NA was found significantly reduced 30 min and 60 min after drug administration. The effect seems to be dose dependent. These data cast some doubts on the relative specificity of action of piridbedil as a dopaminergic activator. 14 references. (Author abstract)

197869 Ross, Svante B.; Gosztonyi, Tamas; Renyi, Anna Lucia. Research and Development Laboratories, Astra Lakemedel AB, S-151 85, Sodertalje, Sweden **Long-term effects of N-hydroxy-4-chloroamphetamine on the level and accumulation of 5-hydroxytryptamine in the rat brain.** European Journal of Pharmacology (Amsterdam). 28(1):222-224, 1974.

The long-term effects of N-hydroxy-4-chloroamphetamine on the level and accumulation of 5-hydroxytryptamine in the rat brain were studied. N-Hydroxy-4-chloroamphetamine was about equally as 4-chloroamphetamine in decreasing the 5-hydroxytryptamine (5-HT) level in the rat brain 3 days and 2 weeks after i.p. administration. The ED50 values for the hydroxylamine derivative were 18 micromole/kg (3 days) and 65 micromole/kg (2 weeks) and for 4-chloroadmphetamine 25/kg (3 days) and 95 micromole/kg (2 weeks). The two compounds were also very similar in producing sustained decreases in the capacities of crude synaptosome preparations to accumulate 14C-5-HT. 9 references. (Author abstract)

197870 Fuller, Ray W.; Perry, Kenneth W.; Snoddy, Harold D.; Molloy, Bryan B. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Comparison of the specificity of 3-(p-trifluoromethylphenoxy)-N-methyl-3 phenylpropylamine and chlorimipramine as amine uptake inhibitors in mice.** European Journal of Pharmacology (Amsterdam). 28(1):233-236, 1974.

The ability of 3-(p-trifluoromethylphenoxy)-N-methyl-3-phenylpropylamine amine hydrochloride (Lilly 110140) and chlorimipramine to block uptake into serotoninergic and noradrenergic neurons was determined by their antagonism of serotonin depletion in brain by p-chloroamphetamine and norepinephrine depletion in mice heart by 6-hydroxydopamine, respectively. Lilly 110140 blocked serotonin depletion with an ED50 of 0.4mg/kg and had no effect on norepinephrine depletion at doses up to 23mg/kg. Chlorimipramine antagonized both serotonin depletion and norepinephrine depletion with ED50 values of 10mg/kg and 6mg/kg, respectively. 9 references. (Author abstract)

197871 Raiteri, Maurizio; Levi, Giulio; Federico, Rodolfo. Istituo di Farmacologia, Universita Cattolica, Via Pineta

Sacchetti 644, Rome, Italy **d-Amphetamine and the release of 3H-norepinephrine from synaptosomes.** European Journal of Pharmacology (Amsterdam). 28(1):237-240, 1974.

The release of 3H-norepinephrine from rat brain synaptosomes was studied by a superfusion technique which prevents reuptake of the released amine. d-Amphetamine had a minimal stimulatory effect on 3H-norepinephrine release and was a potent uptake inhibitor. It is suggested that d-amphetamine may act primarily by inhibiting norepinephrine reuptake at adrenergic synapses. 13 references. (Author abstract)

197926 Paalzow, Gudrun; Paalzow, Lennart. Department of Pharmacology, University of Uppsala, Box 573, S-751 23 Uppsala, Sweden **Theophylline increased sensitivity to nociceptive stimulation and regional turnover of rat brain 5-HT, noradrenaline and dopamine.** Acta Pharmacologia et Toxicologica (Copenhagen). 34(3):157-173, 1974.

Theophylline sensitivity to nociceptive stimulation and regional turnover of rat brain 5-hydroxytryptamine (5-HT), noradrenaline and dopamine were examined. Theophylline is able to decrease the thresholds of nociceptive stimulation (motor response, vocalization and vocalization afterdischarge), the effects being maximal at 30 minutes after administration. After inhibition of tyrosine hydroxylase with alpha-methyl-p-tyrosine, theophylline was found to decrease the depletion of dopamine brought about by the inhibitor in the telencephalic cortex, indicating a decreased turnover of dopamine in this region. Theophylline was able to accelerate the decrease in noradrenaline concentration in the diencephalon striatum region induced by the enzyme inhibition, indicating an increased turnover of noradrenaline. A relationship between a reduced turnover of dopamine and serotonin in the telencephalic cortex and the theophylline induced decrease of the threshold for vocalization afterdischarge (affective component of the pain reactions) is postulated. It is suggested that the modulation of the vocalization response may be related to the serotonin metabolism in lower brain stem structures. 43 references. (Author abstract modified)

197927 Alhava, Eeva; Mattila, Mauri J. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Dose-dependent differences of amphetamine levels in brain and heart of adult and developing mice.** Acta Pharmacologia et Toxicologica (Copenhagen). 34(3):211-221, 1974.

The amphetamine levels in the brain and heart were determined after an intraperitoneal injection of 50mg/kg to adult and developing mice of three age groups. The peak concentration of amphetamine in both tissues was reached within 30 min. in adult and older age groups of developing mice, and the brain amphetamine level was higher than the heart level. In infant brain the peak amphetamine level was low and only slowly reached within 2 hrs, and the infant heart showed an initial amphetamine level which was as high as in the brain. Comparable doses calculated according to body surface in adults and infants gave approximately equal time course graphs for brain amphetamine, but the infant heart amphetamine was higher than that of adult heart. The slow development of the peak amphetamine level in the infant brain is suggested to result from circulatory factors and the immaturity of the infant brain. 14 references. (Author abstract modified)

197928 Nielsen, M.; Eplov, L.; Scheel-Kruger, J. Central Laboratory Sct., Hans Hospital, DK-4000 Roskilde, Denmark **Protriptyline induced inhibition of the in vivo 3H-noradrenaline synthesis from 3H-L-dopa in the rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 285(1):15-28, 1974.

H-L-dopa was given intraperitoneally, after a peripheral decarboxylase inhibitor Ro4-4602 to male Wistar rats and the effect of protriptyline pretreatment on the formation and metabolism of the brain 3H-catecholamines, dopamine and noradrenaline and all their metabolites was investigated. Protriptyline produced a strong decrease of labelled noradrenaline and its metabolites normetanephrine, free and conjugated 3-methoxy-4-hydroxyphenyl-eneglycol and 3,4-dihydroxyphenyleneglycol 60 and 120 min after 3H-L-dopa. In rats and mice the pretreatment with protriptyline (10 mg/kg, 30 min) induced also a significant decrease in brain 3H-noradrenaline but not 3H-dopamine synthesized from 3H-L-tyrosine. Protriptyline produced no effect on endogeneous dopamine and noradrenaline in the rat or mouse brain. It is indicated that acute treatment with protriptyline inhibits the 3H-noradrenaline formation from 3H-L-dopa. 38 references. (Author abstract modified)

197931 Butcher, Larry L.; Eastgate, Sheila M.; Hodge, Gordon K. Department of Psychology, University of California, 405 Hilgard Avenue, Los Angeles, CA 90024 **Evidence that punctuate intracerebral administration of 6-hydroxydopamine fails to produce selective neuronal degeneration: comparison with copper sulfate and factors governing the deportment of fluids injected into brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 285(1):31-70, 1974.

Evidence that punctate intracerebral administration of 6-hydroxydopamine (6-OHDA) fails to produce selective neuronal degeneration is presented. Extensive neuronal degeneration was seen after intrarubral administration of 6-hydroxydopamine (6-OHDA) even though the cell bodies of the red nucleus contain neither dopamine nor noradrenaline. The rigidity and hypokinesia produced by bilateral 6-OHDA injection into the substantia nigra - ventral tegmental area were very similar to the motor manifestations produced by CuSO4. No dose of 6-OHDA was found which produced neuronal degeneration attributable unequivocally to the action of the drug and affected only those neurons having a particular type of neurotransmitter. It is concluded that specificity of neuron destruction can be achieved with 6-OHDA only to the extent that the drug is injected into brain regions which are neurochemically homogeneous. 54 references. (Author abstract modified)

197939 Barth, N. Department of Pharmacology, University, D-65 Mainz, Obere Zahlbacher Strasse 67, Germany **Arrhythmias evoked by infusion of tricyclic antidepressants and noradrenaline on isolated rabbit hearts.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R3, 1974.

At the 1974 meeting of the German Pharmacological Society, arrhythmiasythmias evoked by infusion of tricyclic antidepressants and noradrenaline on isolated rabbit hearts were reported. Since desipramine (DMI) and doxepin (DOX) caused arrhythmiasythmias in rabbit hearts after sympathetic nerve stimulation, it was investigated if increasing doses of noradrenaline (NA) produced arrhythmias, in hearts perfused with DMI, DOX or iprindole (IP). On each heart two dose mechanical response curves were obtained and then DMI, DOX or IP added to the perfusion fluid. After 20 min the NA infusion scheme was repeated. Once arrhythmias had started they continued at higher doses of NA. Propranolol (PR) inhibited NA-DOX induced arrhythmias No arrh. were caused by NA infusion or by IP plus NA. It is concluded that the arr-

hythmias producing potency of tricyclic antidepressants can be differentiated by the method described. (Journal abstract modified)

197940 Bechtel, W. D. Biochemie, C. H. Boehringer Sohn, D-6507 Ingelheim, Germany **Blood level, excretion, distribution and metabolism of 14C-triflubazam, a new 1,5-benzodiazepine, in mice and dogs.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R6, 1974.

At the 1974 meeting of the German Pharmacological Society, a paper on measurement of blood levels as well as renal and fecal excretion in both mice and dogs after p.o. and i.v. administration of 1mg/kg 14C-triflubazam (WE-352, 1-methyl-5-phenyl-7-trifluoromethyl-1H-1,5-benzodiazepine-2,4-(3H,5H)- ion was presented. In mice the maximum blood level was 112 ng equivalents 14C-WE 352 per g blood, 2 hrs after administration. Ten hrs after oral administration the blood level in dogs reached the maximum of 231 ng/g. The total excretion in mouse and dog studies was 81-86% of the administered radioactivity. The distribution of 14C-WE 352 was studied by whole body autoradiography in mice. A transient accumulation of radioactivity was seen in body fat, cardiac muscle, pancreas, lacrymal glands and gastric and intestinal mucosa. The main metabolic pathways of 14C-WE 352 in mice and dogs were N-demethylation and 4-hydroxylation, 3,4-dihydroxylation and 3-methoxy-4-hydroxylation of the phenyl ring. In the urine hydroxylated metabolites were mainly conjugated. (Journal abstract modified)

197941 Benz, M.; Salzmann, R. no address **The effect of PGE1, PGE2 and PGF2alpha on parasympathetic transmission.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R7, 1974.

At the 1974 meeting of the German Pharmacological Society, the effects of prostaglandins (PG) E1, E2 and F2alpha on ylcholine release at rest and during field stimulation were presented. PGE1, PGE2 and PGF2alpha had no significant effect on the release of acetylcholine. Indomethacin alone or in combination with guanethidine, produced no significant change in the acetylcholine output at rest and during field stimulation. In the ileum of reserpinized animals the release of acetylcholine was slightly reduced by indomethacin. Further experiments were carried out in cats anesthetized with urethane-chloralose. The vagal nerve was stimulated peripherally. PGE1 and PGF2alpha showed only a moderate reduction of the effect of parasympathetic nerve stimulation on blood pressure and heartrate. PGE2 had no effect on these parameters. It is concluded that the prostaglandins E1, E2 and F2alpha do not act as physiological modulators in parasympathetic transmission. (Journal abstract modified)

197942 Burger, A.; Beyl, H. H. Department of Pharmacology, University of Wurzburg, Koellikerstrasse 2, Germany **The effect of dipyridamole on the noradrenaline transport into nerve granules.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282 (Supplement):R14, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of dipyridamole on the noradrenaline transport into nerve granules was reported. After homogenization of bovine splenic nerve trunks noradrenaline (NA) storing granules were prepared by differential centrifugation. Granules suspended in isotonic buffer rapidly lost their NA. ATP-Mg++ (3mM each) prevented this NA loss, while in the presence of ATP-Mg++ and NA partially depleted granules showed a NA net uptake into nerve granules. In the presence of ATP-Mg++ the exchange of granular NA with 3H-NA of the medium was also inhibited by dipyridamole. It is concluded that dipyridamole, like reserpine, inhibits the NA transport across the membrane of NA storing granules. (Journal abstract modified)

197943 Endoh, M.; Schumann, H. J. Institute of Pharmacology, University of Essen, Hufelandstrasse 55, D-4300 Essen, Germany **Beta-and/or alpha-adrenoceptors in the ventricular muscle of the rabbit?** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R18, 1974.

At the 1974 meeting of the German Pharmacological Society, the positive inotropic effect (PIE) of phenylephrine (PE) was reported on the ventricular myocardium of the isolated papillary muscle and of the perfused heart of the rabbit. Reserpine pretreatment did not alter either the intrinsic activity or the pD2 value of PE. The PIE of PE was competitively antagonized by phentolamine but not affected by pindolol. In higher concentrations of PE another component of the PIE appeared which was antagonized by pindolol. The phosphodiesterase inhibitor papaverine enhanced exclusively the PIE evoked by higher concentrations of PE. At the same time it increased the intrinsic activity of PE to that of isoprenaline. It is concluded that in the ventricular myocardium of the rabbit besides beta-adrenoceptors alpha-adrenoceptors are of functional importance for the PIE caused by sympathomimetic amines. (Journal abstract modified)

197944 Graefe, K. H.; Trendelenburg, U. Department of Pharmacology, D 8700 Wurzburg, Koellikerstrasse 2, Germany **Hydrocortisone-induced supersensitivity to noradrenaline in the isolated nictitating membrane as a consequence of an impairment of an O-methylating system with high affinity.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R26, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of hydrocortisone (HC) on the sensitivity of the isolated cat nictitating membrane to (-)-noradrenaline (NA) was presented. HC increased sensitivity whenever the experimental conditions resulted in a high potency of NA; however, block of COMT prevented sensitization by HC. HC antagonized O-methylation by the high affinity system. Calculation of the kinetic constants for HC resistant O-methylation yielded values very similar to those obtained for the low affinity system. Apparently, HC blocks extraneuronal uptake into a high affinity compartment. The sensitizing effect of HC indicates that the concentration of NA at the receptors is influenced by this compartment whenever the concentration of NA is well below the Km of this system, and COMT is intact. (Journal abstract modified)

197945 Gothert, M.; Guth, M.; Bille, U. Department of Pharmacology, University of Hamburg, D-2000 Hamburg 20, Martinistrasse 52, Germany **Influence of halothane on peripheral sympathetic nerves and on the effects of noradrenaline on myocardium.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R26, 1974.

At the 1974 meeting of the German Pharmacological Society, the influence of halothane (H) on the release of noradrenaline (NA) from postganglionic sympathetic nerves on isolated rabbit hearts was reported. In hearts with an intact postganglionic sympathetic nerve supply, H did not alter the NA release in response to submaximal electrical stimulation of the nerves. Contrary to that, H caused a dose dependent decrease in NA output evoked by stimulation of nicotine receptors in sympathetic nerve terminals by acetylcholine, nicotine or DMPP; e.g.,the stimulating effect of acetylcholine

in the presence of atropine was inhibited by H. The influence of H on the positive inotropic and chronotropic effects of NA was studied using electrically driven left guinea-pig atria and spontaneously beating right atria. (Journal abstract modified)

197946 Greven, J.; Jacobs, W.; van Eys, B. Abt. Pharmakologie der Med. Fakultat der Technischen Hochschule Aachen, 51 Aachen, Melatenerstrasse 213, Germany **Glucose release of the rat kidney in vivo after beta-adrenergic stimulation and blockade.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R27, 1974.

At the 1974 meeting of the German Pharmacological Society, glucose release of the kidney from the glucose concentration in the arterial and renal venous plasma and total renal plasma flow in the rat was presented. Net renal glucose release was found in control experiments. The glucose release in the blood was high at low arterial plasma glucose concentration in starved rats and decreased with rising plasma glucose values in fed animals. Epinephrine and isoprenaline but not norepinephrine enhanced plasma glucose levels and increased mean renal glucose production significantly. The enhanced glucose release after isoprenaline could be abolished by propranolol. The glycogen content of the kidney was found to be too small to account for the observed renal glucose release by glycogenolysis. These in vivo data indicate enhanced renal gluconeogenesis after catecholamines. This effect is thought to be mediated by the renal beta-adrenergic receptors. (Journal abstract)

197947 Haeusler, G. Department of Experimental Medicine, F. Hoffmann-La Roche & Co., Ltd., CH-4002 Basle, Switzerland **Sympathetic nerve activity after noradrenaline depletion and its alteration by clonidine.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R29, 1974.

At the 1974 meeting of the German Pharmacological Society, sympathetic nerve activity after noradrenaline depletion and its alteration by clonidine were reported. Cats were injected i.p. with reserpine and alpha-methyl-p-tyrosine (MT); 15 hours after reserpine and the first dose of MT and 2 hours after the second dose, the cats were anesthetized with urethane and prepared for the recording of blood pressure, heart rate and spontaneous sympathetic nerve activity (SSNA). Clonidine reduced or abolished SSNA even after central noradrenaline depletion. In comparison to controls, on an average a threefold higher dose of clonidine was required in order to abolish the augmented SSNA of the pretreated animals. Similar observations were made in rats and in conscious cats. The results indicate a direct stimulation of central alpha-adrenoceptors by clonidine and make it unlikely that the central effect of clonidine on blood pressure is due to a release of noradrenaline from central adrenergic neurons. (Journal abstract modified)

197948 Heubers, H.; Huebers, E.; Heubers, U.; Rummel, W. Department of Pharmacology, University of the Saarland, D-665 Homburg, Germany **Influence of MAO-inhibitors on the intestinal absorption of biogenic amines.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282 (Supplement):R36, 1974.

At the 1974 meeting of the German Pharmacological Society, the intestinal absorption of tyramine and analogous amines (5-hydroxytryptamine, D-amphetamine and L-amphetamine) and the interference by monoamine oxidase (MAO) with their absorption was reported. Rat jejunal segments were used in vitro. Complete inhibition of the MAO by pargyline resulted in a marked increase in the tyramine content of the absorbate while there was no influence on the appearance of the other amines. No influence of tyramine, 5-hydroxytryptamine and D-amphetamine on water, electrolytes and glucose absorption was observed. By contrast the stereoisomer L-amphetamine diminished these parameters by 50-80%. (Journal abstract modified)

197950 Keller, H. H.; Bartholini, G. Department of Experimental Medicine, F. Hoffmann-La Roche & Co., Basle, Switzerland **Thyrotropin-releasing hormone: activation of cerebral noradrenaline turnover.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R46, 1974.

At the 1974 meeting of the German Pharmacological Society, the activation of cerebral noradrenaline turnover by thyrotropin releasing hormone (TRH) was reported. Thyrotropin releasing hormone (pyroglutamyl-histidyl-prolineamide) injected i.p. into rats, did not modify the content of brain noradrenaline but significantly increased the concentration of the main cerebral metabolite of this amine, 3-methoxy-4-hydroxy-phenylethyleneglycol sulfate (MOPEG), in various brain regions. Dopamine, 5-hydroxytryptamine and their corresponding major metabolites were not changed by TRH. The hormone enhanced the accumulation of cerebral C-14-noradrenaline, but not that of C-14-dopamine, after injection of C-14-tyrosine into one lateral brain ventricle. It appears that TRH activates the turnover of cerebral noradrenaline. The mechanism of this activation is not known; however, it seems to be independent of the hypophyseothyroid axis. (Journal abstract modified)

197954 Kuschinski, K.; Celsen, B. Department of Biochemical Pharmacology, Max-Planck-Institute for Experimental Medicine, D-34 Gottingen, Hermann-Rein-strasse 3, Germany **Kinetics of 14C-dopamine in isolated rat striatal tissue under the influence of morphine.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R54, 1974.

At the 1974 meeting of the German Pharmacological Society, the kinetics of 14C-dopamine in isolated striatal tissue under the influence of morphine were examined. The labeled dopamine showed a high accumulation, compared with the medium, reaching the equilibrium in the tissues after about 30 min. Morphine slowed down the K+ induced release of (14C)-dopamine. Naloxone significantly inhibited this effect of morphine. Results support the assumption that morphine has a direct and specific action on brain dopaminergic neurons. It is suggested that it might lock up the dopamine in the dopamine synthesis and turnover. (Journal abstract modified)

197955 Leitold, M.; Engelhorn, R. Dr. Karl Thomas Gubh, Biologische Forschung, D 795 Biberach an der Riss, Postfach 720, Germany **Pharmacological examinations by an ulcus inhibiting agent (L-S 519).** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):56, 1974.

At the 1974 meeting of the German Pharmacological Society, pharmacological examinations of an ulcus inhibiting agent were reported. In experimental models producing gastric ulcers in rats the agent (5,11-Dihydro-11-(4-methyl-1-piperazinyl)acetyl)-6H-pyrido(2,3-b) (1,4) benzodiazepin-6-one dihydrochloride) shows an inhibitory effect after enteral application. Moreover, a dose dependent reduction or complete depression of the duodenal ulcers provoked by subcutaneous drop infusion of C-terminal tetrapeptide of gastrin together with carbaminoylcholine may be achieved in the same species after oral treatment with L-S-519. Even the perforated duodenal ulcers provoked by cysteamine HCl in rats could be

stopped dose dependently by the compound following peroral application. A protective effect was obtained in mini pigs with duodenal erosions provoked by hyperacidic agents. Other investigations showed that L-S-519 has no psychopharmacological effects. (Journal abstract modified)

197957 Lemmer, B.; Saller, R. Zentrum der Pharmakologie der Universitat Frankfurt, Frankfurt, Germany **Influence of propranolol and practolol on the turnover of noradrenaline in the rat heart.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R57, 1974.

At the 1974 meeting of the German Pharmacological Society, the influence of propranolol and practolol on the turnover of noradrenaline (NA) in the rat heart was reported. Male Wistar rats were kept under controlled conditions of light and darkness. In the period of illumination the acute effects of injections of propranolol and practolol on the cardiac turnover of noradrenaline was determined by injection of NA. Propranolol caused no or minor effects on the turnover in concentrations of 0.001-0.1mmoles/kg, whereas higher doses decreased the turnover concomitantly with toxic signs from the CNS (seizures, death). The endogenous noradrenaline content was not changed by either concentration of propranolol. Practolol in equimolar concentrations did not influence the NA turnover, but, like an indirectly acting sympathomimetic drug, released NA. (Journal abstract modified)

197958 Lindmar, R.; DeSantis, V. P. Department of Pharmacology, University of D-65 Mainz, Obere Zahlbacher Strasse 67, Germany **The significance of noradrenaline and adrenaline as adrenergic transmitters in the chicken.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R58, 1974.

At the 1974 meeting of the German Pharmacological Society, the significance of noradrenaline (NA) and adrenaline (A) as adrenergic transmitters in the chicken were reported. In isolated, perfused chicken hearts stimulation of the right sympathetic nerves and tyramine caused an output of NA and A. The NA/A in the perfusates was similar to that of the heart. Acetylcholine in the presence of atropine did not evoke an output of catecholamines. Plasma levels of NA and A were obtained from blood taken from the left ventricle of chickens anesthetized with hexobarbital. Application of NA and A was found to cause their accumulation in the neuronal store available for release. Thus both NA and A are transmitters in peripheral adrenergic nerves of the chicken. The high plasma level of A indicates that this adrenergic transmitter may be synthesized in the adrenal medulla and transported via the circulation to the peripheral nerves. (Journal abstract modified)

197959 Loffelholz, K. Department of Pharmacology, University, D-65 Mainz, Obere Zahlbacher Strasse 67, Germany **Effects of sodium, ouabain and DMPP on the neuronal efflux of noradrenaline.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R59, 1974.

At the 1974 meeting of the German Pharmacological Society, the effects of sodium, ouabain and DMPP on the neuronal efflux of noradrenaline were reported. Rabbits were pretreated with pargyline and with reserpine in order to allow exogenous noradrenaline (NA) to accumulate in the axoplasm of adrenergic neurones. After this pretreatment perfusion of isolated hearts with NA for 1 h is sufficient to cause an equilibrium of NA concentrations between extracellular and intraneuronal compartments. During the subsequent washout of NA, the amine left the adrenergic neuron with a neuronal efflux that declined simply exponentially. Na+ free perfusion or Na+ deprivation or ouabain caused a 5-17 fold increase in rate of efflux. DMPP had the same effect as Na+ free perfusion; the DMPP evoked release of NA did not show characteristics of nicotinic release of NA, such as Ca++ dependency and autoinhibition. It is emphasized that the neuronal efflux did not decline simply exponentially after facilitation evoked by Na+ deprivation, ouabain or DMPP as was found when the efflux was not facilitated. Thus facilitation unmasked at least one NA compartment subsequent to the first intraneuronal compartment. (Journal abstract modified)

197960 Lullmann-Rauch, R.; Reil, G. -H. Department of Pharmacology, University of Kiel, D 23 Kiel, Hospitalstrasse 4-6, Germany **Dose-dependence of chlorphentermine-induced ultrastructural alterations in rat.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R60, 1974.

At the 1974 meeting of the German Pharmacological Society, the dose dependence of chlorphentermine induced ultrastructural alterations in the rat were reported. In short-term experiments, lymph nodes and peripheral blood cells of rats were examined 24 hours after p.o. application of a single dose of chlorphentermine. A dose of 10mg/kg already produced lamellated inclusions in a significant number of lymphocytes and plasma cells in lymph node and of lymphocytes in peripheral blood. This number increased with increasing dosage. In long-term experiments,rats received chlorphentermine with the drinking water. In some animals the number of alveolar macrophages was augmented. In all animals the vast majority of alveolar macrophages present had changed into foam cells. Lamellated or crystalloid inclusions were found in many cells of lymph node and of retinal pigment epithelium. The findings indicate that for the rat the minimum dose producing the side-effect in question is within the range of the ED25 with respect to the anorectigenic action, and exceeds the therapeutic dosage for humans only by a factor of 10. (Journal abstract modified)

197961 Magour, S.; Coper, H.; Fahndrich, Ch. Institute of Neuropsychopharmacology, Free University of Berlin, D 1 Berlin 19, Ulmenallee 30, Germany **Studies on the uptake of d-amphetamine by rat cerebral cortex slices.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R62, 1974.

At the 1974 meeting of the German Pharmacological Society, the characteristics of the uptake mechanism of d-amphetamine by rat cerebral cortex slices in vitro were reported. The overall uptake in tissue slices was increased and the tissue to medium ratio (T/M) was decreased. Nitrogen atmosphere, 2,4 dinitrophenol and potassium cyanide inhibited the accumulation of d-amphetamine by 27%, 37% and 16% respectively suggesting the involvement of a metabolically dependent process. Epinephrine and norepinephrine significantly increased the accumulation of d-amphetamine in cortex slices by 26% and 33% respectively. These findings support the hypothesis that amphetamine may enhance its transport system indirectly through elevation of the concentration of these catecholamines in vivo. (Journal abstract modified)

197962 Matthaei, H.; Philippu, A. Department of Pharmacology, University of Wurtzburg, Koellinkerstrasse 2, Germany **Uptake of neurotransmitters into subcellular particles of the caudate nucleus.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R63, 1974.

At the 1974 meeting of the German Pharmacological Society, the uptake of neurotransmitters into subcellular particles of the caudate nucleus was reported. Synaptic vesicles

were isolated by differential centrifugation and incubated with 14C-5lhydroxytryptamine (5-HT), 14C-gamma-aminobutyric acid (GABA) or 14C-histamine (H) at various temperatures. At 25 degrees C the uptake of 5-HT and GABA was strongly enhanced in the presence of ATP-Mg++, while the influx of H into the vesicles was not influenced. At 25 degrees C the enhancing effect of ATP-Mg++ on the influx of 5-HT or GABA was abolished. Likewise, addition of ATP-Mg++ did not activate the uptake of these agents into vesicles submitted to osmotic lysis prior to incubation. At 37 degrees C and in the presence of ATP-Mg++ the vesicular 5-HT content was maximal after incubation for 2.5min. It is concluded that GABA is taken up into separate subcellular particles which are more thermostable than those which take up biogenic amines. (Journal abstract modified)

197963 Meyer, D. K. Department of Pharmacology, University of Freiburg i.Br., D-7800 Freiburg i.Br., Katharinenstrasse 29, Germany **Effect of serotonin on water intake and renin-angiotensin system in rats.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R65, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of serotonin (5-HT) on water intake and renin - angiotensin system in rats were reported. 5-HT caused a highly significant increase in plasma concentration of renin and angiotensin I, the time course of which correlated to the time of greatest water intake. Nephrectomy abolished the 5-HT induced drinking. The beta-receptor blocker (+-) propranolol diminished the drinking and the stimulation of the renin - angiotensin system induced by 5-HT. Camphidonium i.m.,a ganglionic blocking agent of the quarternary amine group, similarly attenuated 5-HT induced drinking as well as the response of the renin - angiotensin system. The following hypothesis is suggested as an explanation of the dipsogenic activity of 5-HT: the drinking observed after 5-HT is it least partially brought about by a stimulation of the renin - angiotensin system. This stimulation of the renin - angiotensin system is mediated in part by the sympathetic nervous system. (Journal abstract modified)

197964 Montel, H.; Weber, F. Institute of Pharmacology, University of Essen, Hufelandstrasse 55, D-4300 Essen, Germany **Influence of morphine on the release of noradrenaline from brain slices.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R67, 1974.

At the 1974 meeting of the German Pharmacological Society, in slices of the rat brain cortex preincubated with (-)-3H-noradrenaline, the influence of morphine on the efflux of tritium was investigated. The spontaneous outflow of tritium was not changed by morphine and by naloxone. Electrical field stimulation accelerated tritium outflow. The overflow evoked per pulse decreased as the frequency of stimulation was increased from 0.3to 3 Hz, but remained approximately constant when it was further increased to 10 Hz. At frequencies of 0.3, 1 and 3 Hz, but not at 10 Hz, morphine depressed the stimulation induced overflow of tritium. Naloxone did not change the response to stimulation. In the presence of naloxone, morphine did not diminish, and morphine even enhanced, the stimulation induced overflow of tritium. It is concluded that morphine through an action on specific opioid receptors inhibits the release of transmitter from cerebrocortical noradrenergic neurones evoked by nerve impulses. (Journal abstract modified)

197965 Mohler, H.; Patel, A.; Balazs, R. Department of Experimental Medicine, F. Hoffmann-La Roche & Co., Basel, Switzerland **On the mechanism of action of gamma-hydroxybutyric acid: lack of conversion to GABA in mouse brain in vivo.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R67, 1974.

At the 1974 meeting of the German Pharmacological Society, the degradation of labelled gamma-hydroxybutyric acid (GHB) in mouse brain was reported. The specific radioactivity (SA) of glutamine (GLN), glutamate (GLU), aspartate (ASP) and gamma-aminobutyric acid (GABA) was determined in whole brain. With time the radioactivity in the amino acid fraction varied from 7% to 45% of the total radioactivity; the remaining part was found mainly in unmetabolized GHB. In the amino acid fraction 90% of the radioactivity was represented by labelled ASP, GLU and GLN. The GABA fraction however contained only 0.01% to 0.05% of the overall radioactivity. The high specific radioactivity of ASP, GLU and GLN as compared to that of GABA indicates predominant degradation of GHB. It is concluded that GABA is not a major metabolite of GHB. This result suggests that a direct formation of GABA is unlikely to contribute to the hypnotic action of GHB. (Journal abstract modified)

197966 Nedergaard, O. A. Instit. of Pharmacology, Odense University, Odense, Denmark **Effect of nicotine and nicotine monomethiodide on vascular adrenergic neuroeffector transmission.** Archives of Pharmacology (Berlin). 282(Supplement):R69, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of nicotine and nicotine monomethiodide on vascular adrenergic neuroeffector transmission was reported. Nicotine (N) and nicotine monomethiodide (NMMI) potentiated the constrictor response of the rabbit isolated pulmonary artery elicited by electrical field stimulation of postganglionic sympathetic neurones. The potentiation was reversible and no development of tachyphylaxis was seen with N. N induced potentiation was characterized by an initial transitory peak, while NMMI enhanced the contractions in a monophasic manner. Hexamethonium and (+) - tubocurarine prevented the potentiation caused by N, while hexamethonium had no effect on the NMMI induced enhancement. It is concluded that N and NMMI increase the nerve stimulation induced release of transmitter from adrenergic neuron terminals. It is unlikely that N and NMMI enter the neuron by means of the NA uptake mechanism. It is suggested that N probably acts on receptors localized on the outer surface of the neuron. (Journal abstract modified)

197968 Pleul, O. Department of Clinical Pharmacology, Free University of Berlin, D-1000 Berlin 45, Hindenburgdamm 30, Germany **On the action of oxotremorine on the cholinergic system of the rat brain.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R75, 1974.

At the 1974 meeting of the German Pharmacological Society, the action of oxotremorine on the cholinergic system of the rat was reported. In rats, oxotremorine (OT) produces anticholinesterase like symptoms, tremor, salivation, diarrhea, and chromodacryorrhea. After OT as well as after anticholinesterases the acetylcholine (ACh) accumulated in brain. The activity of the choline (Ch) acetyltransferase is not altered by OT. Therefore the incorporation of radiolabelled Ch into ACh of rat brain after OT has been studied. Cortex and stem ganglia were separated and the ACh in these areas was fractionated in free, labile bound, and stable bound ACh. The overall increase of ACh is higher in the cortex than in the stem. The incorporation of radiolabelled Ch into ACh is diminished. It is concluded that the reduction of the ACh

synthesis is a consequence of an inhibition of the transmitters breakdown which results in the increased concentration. (Journal abstract modified)

197969 Rauws, A. G. Laboratory of Pharmacology, National Institute of Public Health, P.O. Box 1, Bilthoven, the Netherlands. **Treatment of experimental imipramine intoxication by interrupting enteral cycles with activated charcoal.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R78, 1974.

At the 1974 meeting of the German Pharmacological Society, the treatment of experimental imipramine (IP) and desipramine (DMI) intoxication by interrupting enteral cycles with activated charcoal was reported. It was found that the entero-hepatic cycle was not as intensive as expected. The source of the high concentrations of IP and DMI in duodenal contents was the stomach. Concentrations well above 200 micrograms/g were found. It is concluded that an intensive gastro enteral cycle was operative. New experiments, taking account of a gastroenteral cycle, were carried out and will be discussed. (Journal abstract modified)

197970 Schrold, J. Institute of Pharmacology, University of Odense, DK-5000 Odense, Denmark **Effect of tropolone on vascular sympathetic neuroeffector transmission.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R86, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of tropolone on vascular sympathetic neuroeffector transmission was reported. After a latency period, the COMT inhibitor tropolone (T) blocked increasingly the contractile response of isolated rabbit pulmonary artery elicited by electrical field stimulation. T also contracted the artery. These effects were irreversible. Abother COMT inhibitor, U-0521 (3'4'-dihydroxy-2-methyl-propiophenone), did not cause these effects. Phentolamine elicited a reversible equilibrium block with rapid onset. T which had been subjected to oxygenated physiological salt solution for 5 hrs accelerated the development of neurogenic block compared to a freshly prepared solution of T. This suggests that the blocking effect may in part be due to a breakdown product of T. Field stimulation induced outflow of tritium from arteries preloaded with 3H-noradrenaline was not changed by T. Initially, T did not alter the cumulative concentration contraction response curves of exogenous noradrenaline, acetylcholine and serotonin. (Journal abstract modified)

197971 Scholtysik, G. Biological and Medical Research Division, Sandoz Ltd., Basle, Switzerland **Inhibition of effects of accelerator nerve stimulation in cats and rabbits by BS: 100-141 and guanabenz.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R86, 1974.

At the 1974 meeting of the German Pharmacological Society, the inhibition of effects of accelerator nerve stimulation in cats and rabbits by BS 100-141 and guanabenz were reported. In pithed cats, electrical stimulation of spinal segments C7 and T1 induced frequency dependent increases in heartrate and contractions of the nictitating membrane due to increase of the sympathetic nerve activity. BS 100-141 (BS) and guanabenz (G) did not influence resting heartrate, but inhibited dose dependent stimulation induced increases in heartrate, resulting in a shift to the right of the frequency response curve. BS and G had no effect on the nictitating membrane response. Both drugs induced dose dependent transient increases in blood pressure due to alpha-adrenoceptor stimulation. A close correlation was found between pressor effects and inhibition of accelerator nerve stimulation. In order to see whether the observed inhibitory effects of BS and G were related to an inhibition of noradrenaline (NA) release from adrenergic nerve endings, studies were made on isolated perfused rabbit hearts. The postganglionic adrenergic nerves to the heart were stimulated and the output of NA in response to stimulation determined. BS and G induced a concentration dependent inhibition of NA release in response to nerve stimulation. (Journal abstract modified)

197972 Schultz, J. Institute fur Toxikologie der Universitat, D-7400 Tubingen, Lothar-Meyer-Bau, Wilhelmstrasse 56, Germany **Adenosine 3', 5'-monophosphate in cerebral cortical slices from guinea pig and rat: effect of benzodiazepines.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R89, 1974.

At the 1974 meeting of the German Pharmacological Society, the effects of benzodiazepines on adenosine 3',4'-monophosphate (cyclic AMP) in cerebral cortical slices from the guinea pig and rat were reported. Several benzodiazepines, diazepam, chlordiazepoxide, desmethyl-diazepam, methyloxazepam and oxazepam, potentiate the accumulation of adenosine 3',5'-monophosphate (cyclic AMP) elicited by histamine and histamine/noradrenaline in cerebral cortical slices of guinea pig. In addition these drugs increase cyclic AMP levels in control incubations by about 100%. When adenosine is used to stimulate cyclic AMP formation, only diazepam, desmethyldiazepam and methyloxazepam are increasing cyclic AMP levels significantly over respective controls. (Journal abstract modified)

197973 Starke, K. Institute of Pharmacology, University of Essen, Hufelandstrasse 55, D-4300 Essen, Germany **Influence of oxymetazoline and phentolamine on noradrenaline (NA) release caused by electrical stimulation, potassium, tyramine and dimethylphenylpiperazine (DMPP).** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R95, 1974.

At the 1974 meeting of the German Pharmacological Society, the influence of oxymetazoline and phentolamine on the response to electrical stimulation was compared with their effect on release by K+, tyramine and dimethylphenylpiperazine (DMPP) was reported. Oxymetazoline decreased and phentolamine increased, the outflow of NA evoked by 50 mM K+. In hearts preperfused with noradrenaline (NA), oxymetazoline diminished, and phentolamine enhanced, K+ induced overflow of both NA and total tritium. At concentrations which modified the response to K+, oxymetazoline and phentolamine did not change the overflow of NA evoked by tyramine. Either drug diminished NA overflow induced by DMPP. It is concluded that oxymetazoline depresses NA release evoked by K+, or orthodromic action potentials through activation of neuronal alpha-receptors, followed by inhibition of electrosecretory coupling. Phentolamine blocks the analogous inhibitory effect of liberated NA and thus enhances release. (Journal abstract modified)

197974 Theiss, P.; Papeschi, R. Department of Neuropharmacology, Max-Planck Institute for Psychiatry, 8000 Munchen 40, Kraepelinstrasse 2, Germany **Turnover of biogenic amines after acute and chronic morphine treatment in rats.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R98, 1974.

At the 1974 meeting of the German Pharmacological Society, the turnover of brain monoamines, dopamine (DA), noradrenaline (NA) and serotonin (5-HT) was measured after

acute morphine treatment or chronic morphine pellet implantation in groups of rats with increasing degree of dependence (and tolerance). The rate of accumultion after probenecid of homovanillic acid (HVA) and 5-hydroxyindoleacetic acid (5-HIAA) was increased by both acute s.c. injections or chronic pellet implantations; however, the increased acid production was already high in animals with the lowest degree of dependence. In the latter case the accumulation of 5-HIAA at 2 hours after probenecid was even not different from that of controls. When the same dose of morphine was injected s.c. 3 times a day over a period of 8 days, this drug was still able to increase the accumulation of 5-HIAA and especially of HVA. The turnover of brain DA, NA and 5-HT after chronic and acute morphine was also studied by inhibition of synthesis with alpha-propyl-dopacetamide (H 22/54) or alpha-methyl-para-tyrosine (AMT). (Journal abstract modified)

197975 Todzy, I.; Becker, W. Institute of Neuropsychopharmacology, Free University Berlin, D1 Berlin 19, Ulmenallee 30, Germany **Alteration of the effects and the metabolism of d-amphetamine by ethanol.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R99, 1974.

At the 1974 meeting of the German Pharmacological Society, the parahydroxylation of amphetamine by rat liver microsomes under the influence of ethanol was reported. A new photometric method has been used which bases on extraction of p-OH-amphetamine into n-amylalcohol: petroleum benzine at pH 7.0and reaction with Folin's phenol reagent giving a blue color. Ethanol inhibited the parahydroxylation in an apparent competitive manner. In vivo, ethanol slightly prolonged the hypermotility induced by amphetamine. Stereotypic behavior (licking, head movements, paw movements) and reactivity on external stimuli (air blow) were not only prolonged but also intensified. (Journal abstract modified)

197985 Westfall, T. C. Department of Pharmacology, University of Virginia, School of Medicine, Charlottesville, VA 22903 **Effect of nicotine and other drugs on the release of 3H-norepinephrine and 3H-dopamine from rat brain slices.** Neuropharmacology (Oxford). 13(8):693-700, 1974.

The effect of nicotine and other drugs on the release of 3H-norepinephrine and 3H-dopamine from rat brain slices were examined. Nicotine produced a significant increase in the release of 3H-NE from incubated slices prepared from rat hypothalamus, cortex, and cerebellum. The effect on the hypothalamus was much greater than on the other two regions. Nicotine also produced a release of 3H-NE from superfused slices of rat hypothalamus which was dependent upon extracellular calcium and reduced by pior addition of hexamethonium or acetylcholine to the superfusion medium. Nicotine produced a similar release of 3H-DA from rat striatal slices. This effect was an reduced by acetylcholine, methacholine, hexamethonium and lidocaine. Morphine and cocaine were without effect while phenoxybenzamine produced a significant increase in the release of 3H-DA induced by nicotine. It is concluded that nicotine can release monoamines from central tissue; the effect is dependent upon extracellular calcium and is produced by an action on classical nicotinic receptors. 27 references. (Author abstract modified)

197986 Soubrie, P.; Wlodaver, C.; Schoonhoed, L.; Simon, P.; Boissier, J. R. Unite de Recherches de Neuropsychopharmacologie de l'Inserm 2, rue d'Alesia, 75014 Paris, France **Preselection of animals in studies of anti-anxiety drugs.** Neuropharmacology (Oxford). 13(8):719-728, 1974.

The preselection of animals in studies of antianxiety drugs is discussed. The classification of the behavior of rats in the open field test into two groups, which differ with respect to the emotionality level of the animal is presented. The distribution of the number of rats in each group was stable and reproducible over a 3 month period. The rats of the emotional group was stable and reproducible over a 3 month period. The rats of the emotional group were more susceptible to gastric lesions produced by immobilization. The rats which were more susceptible to lesions also showed more behavior deterioration upon repeated trials in a heated floor maze. The favorable action benzodiazepines was group dependent. Dexamphetamine (tested on restraint ulcer), imipramine and chlorpromazine (tested on the heated floor maze) acted independently of the rats' emotionality. A relationship between emotionality and differential susceptibility to drugs is discussed. The preselection of animals differential susceptibility to drugs is discussed. The preselection of animals in studies of antianxiety drugs is considered as a possible way to more precise results and as a possible approach to a better understanding of the mechanism of action of anxiolytics. 37 references. (Author abstract modified)

197989 Anderson, Rebecca J.; Raines, A. Department of Pharmacology, Georgetown University School of Medicine and Dentistry, Washington, DC 20007 **Selective diphenylhydantoin suppression of auditory evoked potentials in the cat cerebellar cortex.** Neuropharmacology (Oxford). 13(8):749-754, 1974.

The selective suppression of auditory evoked potentials by diphenylhydantoin in the cat cerebellar cortex is reported. Diphenylhydantoin reduced auditory responses produced by a 2800 Hz 60 dB tone in all three cerebellar areas, 5mg/kg being below threshold and doses of 20mg/kg or more completely abolishing the response. Diphenylhydantoin seemed to have no effect on spontaneous cerebellar activity. 10 references. (Author abstract modified)

197990 Guha, D.; Pradhan, S. N. Department of Pharmacology, Howard University, College of Medicine, Washington, DC 20001 **Effects of mescaline, (delta9)-tetrahydrocannabinol and pentobarbital on the auditory evoked responses in the cat.** Neuropharmacology (Oxford). 13(8):755-762, 1974.

Effects of mescaline, delta9-tetrahydrocannabinol (THC) and pentobarbital were studied on the peak latency, area and amplitude of the waves (positive P1 and negative N1) of the averaged auditory evoked potentials in restrained conscious cats. Mescaline caused a significant increase in peak latency and amplitude of these waves. The onset of these changes was within 10-40 min and their duration ranged between 90-180 min. THC also caused a marked increase in peak latency, area and amplitude while Tween 80 caused slight and variable effects. The effects of THC had its onset within 40-105 min and lasted for more than 120-180 min. Pentobarbital also caused an increase in the peak latency area and amplitude of these waves within 5-7 min. The peak effect occurred within 10-15 min and lasted for more than 100-120 min. These effects of the hallucinogens, mescaline and THC thus appear to resemble those of pentobarbital, a central nervous system depressant; however the mechanism of their actions differs. 29 references. (Author abstract)

197991 Maickel, R. P.; Maloney, G. J. Department of Pharmacology, Medical Sciences Program, Indiana University, Bloomington, IN 47401 **Taste phenomena influences on stimulation of deprivation-induced fluid consumption of rats.** Neuropharmacology (Oxford). 13(8):763-767, 1974.

The dipsogenic actions of barbital and chlordiazepoxide are selectively influenced by the taste of the consummatory fluid presented to deprived rats. The potency of barbital as a consummatory stimulant is reduced relative to distilled water or tartaric acid by the use of a pleasant tasting fluid, saccharin. The potency of chlordiazepoxide as a dipsogenic agent was reduced by the use of either tartaric acid or saccharin as a consummatory fluid as compared to water. Promazine depressed deprivation-induced fluid consumption with a similar potency regardless of the consummatory fluid used. 11 references. (Author abstract)

197993 Miller, J. J.; McLennan, H. Department of Physiology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **The action of bicuculline upon acetylcholine-induced excitations of central neurons.** Neuropharmacology (Oxford). 13(8):785-787, 1974.

The action of bicuculline upon acetylcholine induced excitations of central neurons was examined. The electrophoretic application of a quaternary ammonium derivative of bicuculline to single neurones in amounts adequate to prevent their inhibition by gamma-aminobutyric acid delivered from another barrel of the electrode assembly, causes a marked enhancement of the excitation of the cells induced by acetylcholine. This effect is consistent with the report that bicuculline is active as an anticholinesterase. 15 references. (Author abstract)

197994 Gaillard, J. M.; Herkert, B.; Tissot, R. Clinique Psychiatrique Universitaire de Geneve, 1225 Chene-Bourg, Geneve, Switzerland **Reversal of the reserpine electroencephalographic synchronization in the rabbit by parachlorophenylalanine.** Neuropharmacology (Oxford). 13(8):789-793, 1974.

Reversal of the reserpine electroencephalographic synchronization in the rabbit by parachlorophenylalanine (pCPA) is reported. In the rabbit, reserpine induced an initial period of synchronization of the electroencephalogram which lasted about 30 min and was followed by a sustained pattern of electrical activation. Pretreatment with p-CPA reversed the initial reserpine synchronization, which was replaced by a continuous and very regular pattern of electrical activation. The sleep pattern following injection of reserpine is interpreted as related to a release of 5-hydroxytryptamine (5-HT) in active sites and therefore available for synaptic transmission. This release of 5-HT predominates at the beginning of reserpine action and the subsequent activated period could be related to a dominance of catecholaminergic mechanisms. 9 references. (Author abstract)

198015 Hollunger, Gunnar; Persson, Sven-Ake. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The formation in vivo of 3,4-dihydroxyphenylalanine (DOPA) from 3-hydroxy-DL-phenylalanine (m-tyrosine).** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(5):391-398, 1974.

The formation of 3,4-dopa from m-tyrosine in vivo is demonstrated in the rat. The kinetic aspects of DOPA accumulation in the brain after central and peripheral inhibition of the l-aromatic amino acid decarboxylase are considered. It is concluded that the excess dopa accumulation after administration of m-tyrosine is due to the uptake from the blood of dopa generated in the liver. This exogenous dopa is shown to be much less exposed to brain decarboxylase than dopa generated in the brain. The possibility that the pharmacological effects of m-tyrosine can at least partly be explained by dopamine generation from dopa is discussed. 25 references. (Author abstract)

198021 Karler, Ralph; Cely, William; Turkanis, Stuart A. Dept. of Pharmacology, Univ. of Utah College of Medicine, Salt Lake City, UT 84132 **Anticonvulsant properties of delta9-tetrahydrocannabinol and other cannabinoids.** Life Sciences (Oxford). 15(5):931-947, 1974.

Anticonvulsant properties of delta9-tetrahydrocannabinol (delta9-THC) and other cannabinoids were tested in mice. Anticonvulsant doses of the drug markedly lower body temperature in mice at an ambient temperature of 22 degrees C, but there is little such effect at 30 degrees C. The anticonvulsant properties are as follows: the drug abolishes hind limb extension in a maximal electroshock (MES) test, elevates both the MES (extensor) and 6 Hz electroshock thresholds, exerts no effect on the 60 Hz electroshock threshold and enhances minimal seizures caused by pentylenetetrazol. All anticonvulsant properties studied, with the exception of the 60 Hz electroshock threshold, were unaffected by the hypothermia resulting at 22 deg C. Chronic treatment with delta9-THC results in the development of tolerance. The four principal naturally occurring cannabinoids, delta9-THC, delta8-THC, cannabinol and cannabidiol, display anticonvulsant activity, as does the major primary metabolite of delta9-THC, 11-hydroxy-delta9-THC. The results of a study of the relative motor toxicity and anticonvulsant activity of the cannabinoids demonstrate that these properties are at least partially separable among the various agents. 32 references. (Author abstract modified)

198025 Modigh, K. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Effects of social stress on the turnover of brain catecholamines and 5-hydroxytryptamine in mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(2):97-105, 1974.

The effects of social stress on the turnover of brain catecholamines and 5-hydroxytryptamine (5-HT) in mice were examined. The turnover of brain dopamine (DA), noradrenaline (NA) and 5-HT was estimated in such isolated, grouped and fighting animals by measuring the rate of depletion of these monoamines after inhibition of their biosynthesis. The animals were given alpha-propyl dopacetamide (H22/54), an inhibitor of tyrosine and tryptophan hydroxylase, or the methylester HCl of alpha-methyl-tyrosine (H44/68), an inhibitor of tyrosine-hydroxylase. The H22/54 induced depletion of NA was similar in the isolated and grouped animals but was accelerated in the fighting animals. The rate of depletion of DA or 5-HT, after H22/54, did not differ significantly among the isolated, grouped or fighting animals. The H44/68 induced depletion of NA in the grouped animals was faster than that in isolated animals, while the NA depletion in the fighting animals was faster than that in grouped animals. 23 references. (Author abstract modified)

198026 Edelfors, Sven. Department of Pharmacology, University of Copenhagen, 20 Juliane Maries Vej, DK-2100 Copenhagen, Denmark **Effects of psychotropic drugs on the incorporation of glucose-14C into amino acids of the rat brain.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(2):115-120, 1974.

The effects of chlorpromazine, 25mg/kg subcutaneously, nialamide, 50mg/kg i.p.,and imipramine, 100mg/kg i.p.,respectively, on the glucose and amino acid metabolism of the central nervous system of the rat were examined. Thirty minutes after the injection of U-14C-D-glucose the total amount and specific activity of the amino acids, aspartic acid, glutamic acid, glutamine, alanine, and gamma-aminobutyric acid from the brain were determined. With imipramine the

study was extended to include 5, 15, 30, 45, and 90 min after injection of U-14C-D glucose. Imipramine reduced the glucose concentration, but brought about an increase in the specific activity of glucose. Chlorpromazine reduced the specific activity of the amino acid tested. Nialamide increased the specific activity of aspartic acid and gamma-aminobutyric acid. 8 references. (Author abstract modified)

198027 Smith, Donald F. Psychopharmacology Research Unit, Statshospitalet, 8240 Risskov, Denmark **The effect of NH4Cl on polyuria and polydipsia during prolonged lithium administration in the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(2):121-129, 1974.

The effect of NH4Cl on polyuria and polydipsia during prolonged lithium administration in the rat was examined. Polyuria and polydipsia developed in rats given water to drink and fed a diet containing lithium which maintained their serum lithium level between 0.45 and 0.65meq/1 for 2 weeks. Polyuria and polydipsia were completely prevented and partially cured in rats given the lithium containing diet and solutions of NH4Cl. Polyuria and polydipsia were partially prevented but not cured in rats given water and fed a diet containing lithium and NH4Cl. The possible mechanisms responsible for the effects of NH4Cl on polyuria and polydipsia in the rats given lithium are discussed. 15 references. (Author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

192951 Cox, Tom. Dept. of Psychology, Univ. of Nottingham, University Park, Nottingham NG7 2RD, England **The effects of physostigmine during the acquisition of avoidance behaviour as a function of the intersession interval.** Quarterly Journal of Experimental Psychology (Cambridge). 26(3):387-394, 1974.

The time dependent (intersession interval) effects of physostigmine are studied by using the acquisition of avoidance behavior in the shuttlebox and incorporating adequate control conditions. The change in the performance of the control rats over two sessions was found to be a U-shaped function of the interval between sessions. The change in performance of rats injected with physostigmine prior to the second session was also found to be a U-shaped function of the intersession interval, although the drug was shown to impair avoidance behavior. These results are consistent with those of Hamburg and of Biederman, and support the general contention that cholinergic mechanisms in the brain are involved in the control of avoidance and escape behavior in the rat. They do not, however, necessarily support the hypothesis advanced by Deutsch to describe a biochemical basis of learning and memory, especially if it is used to explain the effects of cholinesterase inhibitors on avoidance behavior in the shuttlebox. 25 references. (Author abstract modified)

192952 Warburton, D. M. Dept. of Psychology, University of Reading, Earley Gate, Whiteknights, Reading FG6 2AL, England **The effects of scopolamine on a two-cue discrimination.** Quarterly Journal of Experimental Psychology (Cambridge). 26(3):395-404, 1974.

To test the hypothesis that if scopolamine is attenuating stimulus sensitivity, increasing the number of relevant cues could partially restore the discrimination performance of the drugged animal, rats were trained with a tone, light, or a tone - light combination as the discriminative stimulus. These groups were tested after doses of scopolamine and it was found that groups trained with a single cue were more sensitive to the drug than double cue groups, although their predrug responding was similar. A similar pattern was found among individuals in the double cue groups in which there was a significant correlation between dependency on a single cue, as shown in transfer tests, and drug sensitivity. These results are interpreted in terms of scopolamine induced changes in stimulus sensitivity produced by a modification of the neural mechanisms controlling attention. 24 references. (Author abstract modified)

193137 Woods, James H.; Tessel, Richard E. Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48104 **Fenfluramine: amphetamine congener that fails to maintain drug-taking behavior in the rhesus monkey.** Science. 185(4156):1067-1069, 1974.

Fenfluramine failed to maintain self-injection behavior in rhesus monkeys that had initiated and maintained responding for cocaine or methohexital. This absence of a positive reinforcing effect could not be attributed to a slow onset of drug effect or to the use of behaviorally inactive doses. Fenfluramine, because of its distinctive properties, may produce fewer problems of human abuse than do amphetamine type agents. 17 references. (Author abstract)

193157 Houser, Vincent P.; Van Hart, Dale A. Psychotropic Drug Laboratory, VA Hospital, Perry Point, MD 21902 **Serotonin and the aversive threshold in rats.** Bulletin of the Psychonomic Society. 3(5B):388-390, 1974.

The effects of p-chlorophenylalanine (p-CPA) and 5-hydroxytryptophan (5-HTP) upon the aversion threshold of the rat were explored using the spatial preference technique. p-CPA had no reliable effects on the aversive threshold or upon motor activity as measured by this technique. 5-HTP, on the other hand, significantly raised the aversion threshold to moderate levels under 95mg/kg and 125mg/kg dosages, while motor activity was reduced under 60mg/kg, 70mg/kg, 95mg/kg, and 125mg/kg dosages. p-CPA (200mg/kg) was able to block both the increased thresholds and reduced motor activity noted after 125mg/kg of 5-HTP. These results are interpreted to suggest that modulation of serotonergic activity has little effect upon the aversion threshold of the rat. 12 references. (Author abstract)

193282 Jurna, I.; Grossmann, W.; Nell, T. Institut fur Pharmakologie und Toxikologie der Univ. d. Saarlandes, D-6650 Homburg/Saar, Germany **Depression by amantadine of tremor induced by reserpine and oxotremorine in the rat.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 280(3):141-152, 1973.

Reserpine and oxotremorine tremor and the effect of amantadine on the tremor activity produced by both drugs were investigated in rats with respect to alpha and gamma motor activity changes. The tremor activity elicited by reserpine is maintained by the alpha motoneurones; the tremor activity developing during an oxotremorine infusion is triggered by the gamma motoneurones. Amantadine abolished the tremor produced by oxotremorine. The tremor activity resulting from an administration of reserpine was inhibited by amantadine in rats with their dorsal roots cut; in rats with intact dorsal roots, tremor activity persisted after reserpine and amantadine. It is concluded that the tremor resulting from reserpine and oxotremorine is caused by an action of the two drugs on different structures of the central nervous system. The antitremor effect of amantadine is discussed. 13 references. (Author abstract modified)

193420 Singh, Jasbir M. Alcoholism Services Unit, Dept. of Psychiatry, Charity Hospital, New Orleans, LA Effect of

apomorphine and nalline on methadone-induced behavioral changes. Toxicology and Applied Pharmacology. 29(1):79, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology in March, 1974, the effect of apomorphine and nalline on methadone induced behavioral changes in mice was reported. Male mice were placed on an activity platform and the circular or edging movement effects (CME) were recorded. After ip administration of methadone, the animals began to move in a circular manner with tails up; the effect of methadone was dose dependent. Prior administration of apomorphine blocked the CME, and the effect was partially blocked by nalline. Some movements were recorded after administration of apomorphine and nalline alone. (Journal abstract modified)

193434 Brophy, Patrick D.; Levitt, Robert A. Div. of Humanities and Social Sciences, Rose-Hulman Institute of Technology, Terre Haute, IN 47803 **Effects of transmitter mimickers at sites of angiotensin-induced drinking in the cat.** Bulletin of the Psychonomic Society. 3(6):432-434, 1974.

A variety of mimickers of synaptic transmitter activation were tested at neural sites in the cat effective for the elicitation of drinking by angiotensin-II. The angiotensin-II was administered in a dose of 1000ng and the mimickers, norepinephrine, epinephrine, isoproterenol, dopamine, 5-hydroxytryptamine and carbachol, in doses of 10mg. None of the putative neurotransmitter agonists elicited water ingestion. The carbachol produced parasympathetic arousal, emotion activation, convulsions and circling behavior. The catecholamines produced drowsiness and sleep. The isoproterenol and 5-hydrosytryptamine were without obvious behavioral effects. The role of the brain synaptic transmitter systems in the mediation of thirst by angiotensin is discussed. 22 references. (Author abstract)

193446 Ankier, Stephen I. Roussel Laboratories Ltd., Medical Department, Roussell House, Wembley Park, Middlesex, HA9 0NF, England **New hot plate tests to quantify antinociceptive and narcotic antagonist activities.** European Journal of Pharmacology (Amsterdam). 27(1):1-4, 1974.

The effects of narcotic, narcotic antagonist and nonnarcotic analgesics on the responses of mice placed on hot plates at different temperatures were investigated. In a 50 degrees Centigrade hot plate test, the antinociceptive activities of narcotic, narcotic antagonist and nonnarcotic analgesics are easily identified and quantified. In a 59 degree Centigrade hot plate test, it is possible to quantify the narcotic antagonist activities of naloxone, nalorphine and pentazocine. 17 references. (Author abstract)

193545 Benton, David; Kyriacou, Charalambos P.; Rick, John T.; Taberner, Peter V. Dept. of Psychology, University College of Wales, Swansea, Wales **Behavioural interactions between imidazoleacetic acid and gamma-hydroxybutyric acid in rats and mice.** European Journal of Pharmacology (Amsterdam). 27(3):288-293, 1974.

Behavioral effects of gamma-hydroxybutyric acid (GHB) and imidazoleacetic acid (IMA) in rats and mice are compared. Mice and rats were injected with hypnotic doses of imidazoleacetic acid and GHB either singly or in combination. GHB was the more potent drug in the rat and IMA, a metabolite of histamine, the more potent drug in the mouse. IMA given prior to GHB produced a potentiation of hypnotic effects in the rat, but when the drugs were given simultaneously or in the reverse order, no potentiation was observed. Since the potentiation was specific to the rat it was proposed that the effect may reflect differences in the activities of histamine metabolizing enzymes between the two species. Pentobarbitone and GHB combinations were also tested, but without potentiation. 27 references. (Author abstract modified)

193546 Clineschmidt, Bradley V.; McGuffin, Jodie C.; Werner, A. Barbara. Merck Institute for Therapeutic Research, West Point, PA 19486 **Role of monoamines in the anorexigenic actions of fenfluramine, amphetamine and p-chloromethamphetamine.** European Journal of Pharmacology (Amsterdam). 27(3):313-323, 1974.

The role of monoamines in the anorexigenic actions of fenfluramine, amphetamine and p-chloromethamphetamine was investigated in the rat. All of the substances used for pretreatment exhibited selectivity; in no instance did an antagonist of fenfluramine also reduce the effect of amphetamine, and vice versa. Results obtained through tests with p-chloromethamphetamine indicate that it cannot be classified as either primarily fenfluramine-like or amphetamine-like in its mode of action. It is concluded that 5-hydroxytryptamine is involved in the anorexigenic effect of high doses of fenfluramine, that catecholamines are important in the action of high dose levels of amphetamine, and that the anorexia which follows low doses of fenfluramine and amphetamine occurs via mechanisms not involving 5-hydroxytryptamine, norepinephrine or dopamine. 29 references. (Author abstract modified)

193548 Jacobs, Barry L. Dept. of Psychology, Princeton Univ., Princeton, NJ 08540 **Effect of two dopamine receptor blockers on a serotonin-mediated behavioral syndrome in rats.** European Journal of Pharmacology (Amsterdam). 27(3):363-366, 1974.

The effect of spiroperidol and pimozide on serotonin mediated behavioral syndromes in rats is reported. Apomorphine produces a behaviorial syndrome in the rat consisting of sniffing, chewing, and locomotion; dopamine receptor blockers spiroperidol and pimozide effectively block this syndrome. L-Tryptophan given to a pargyline pretreated rat produces a syndrome consisting of tremor, rigidity, forepaw treading, and head weaving. This serotonergic syndrome can be blocked by spiroperidol, but pimozide in doses as high as 10mg/kg is ineffective. These data indicate that some dopamine receptor blockers also affect serotonin receptors, whereas others do not. Ratios of dopamine/serotonin blockage are given. 3 references. (Author abstract modified)

193549 Gray, Gary D.; Davis, Harry N.; Dewsbury, Donald A. Dept. of Psychology, university of Florida, Gainesville, FL 32611 **Effects of L-dopa on the heterosexual copulatory behavior of male rats.** European Journal of Pharmacology (Amsterdam). 27(3):367-370, 1974.

Effects of L-dopa on the sexual behavior of 44 adult laboratory rats with and without Ro 4-44602 were evaluated in two experiments. Some influences of L-dopa on the heterosexual copulatory behavior of male rats were observed. L-Dopa and Ro 4-44602 together prolonged the time required for copulation; L-dopa alone produced similar though smaller, nonsignificant effects. Dose dependent increases in time required for copulation were obtained in males treated with both L-dopa and Ro 4-44602. It is suggested that L-dopa acts to inhibit heterosexual copulatory behavior in sexually vigorous males, but the inhibitory effects were not dramatic even using Ro 4-44602. 8 references. (Author abstract modified)

193576 Rosenkrantz, Harris; Braude, Monique C. Mason Research Institute, Worcester, MA 01608 **Acute, subacute and 23-day chronic marihuana inhalation toxicities in the rat.** Toxicology and Applied Pharmacology. 28(3):428-441, 1974.

Acute, subacute, and 23 day toxicities of tetrahydrocannabinol impregnated and nonimpregnated marihuana cigarettes were determined in Fischer rats. Human smoking conditions were similated with a machine. Acute toxicity was manifested by dose related hypothermia, hypopnea, loss of coordination, ataxia, and prostration. Upon removal from the inhalator, high dosed animals were depressed and low dosed animals displayed increased activity rapidly followed by depression. Recovery was nearly complete by 24 hours in the acute trial and by day 6 in the subacute study. Food intake and liver glycogen were increased. In the chronic study, there was a dose related central nervous system (CNS) depression and vocalization in the first week of exposure. During the fourth and last week of exposure, tolerance developed to CNS stimulation in all groups, and animals were either normal or tranquil. Clinical signs were primarily affected in the first week of exposure. Fighting and other behaviors were also observed. 35 references. (Author abstract modified)

193578 Zis, Athanasios P.; Fibiger, Hans C.; Phillips, Anthony G. Department of Psychology, Univ. of British Columbia, Vancouver, British Columbia, Canada **Reversal by L-dopa of impaired learning due to destruction of the dopaminergic nigro-neostriatal projection.** Science. 185(4155):960-962, 1974.

Brain catecholamine projections and conditioned avoidance responding deficits reversed by L-dopa treatment in 18 rats are reported. Rats receiving bilateral stereotaxic injections of 6-hydroxydopamine into the zona compacta of the substantia nigra failed to learn a one way active avoidance response. Small doses of L-dopa in combination with a peripheral decarboxylase inhibitor reversed this impairment. Animals with lesions which acquired the avoidance response during L-dopa administration retained this response when drug treatment was discontinued. These experiments suggest that the dopaminergic nigro-neostriatal projection serves a critical function in the acquisition of learned instrumental responses. The effect on 16 control animals is also discussed. 16 references. (Author abstract modified)

193581 Crabbe, John C., Jr. University of Colorado **Effects of d-amphetamine on learning and memory in inbred and hybrid mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-32524 HC$12.50 MF$4.00 132 p.

Components of memory, consolidation of memory, effects of treatments on memory processes and genetic factors relating to learning and memory are discussed. The effects of amphetamine on learning, memory, and related behavior are reviewed; metabolism and effects of amphetamine on neurotransmitter systems are briefly summarized. Experiment one examined the dose response relationships of d-amphetamine's disruptive effect on the long-term store of memory and proactive facilitatory effect on learning in mice, as compared to those in a group of saline treated Ss. Latencies were not different among the groups, indicating that performance effects of amphetamine were not responsible for the observed maze retention deficits. Some mice were assigned to naive groups and treated exactly as were the initially trained Ss. Naive Ss receiving 1.0mg/kg d-amphetamine were significantly improved over the naive saline group in trials and total errors to criterion. The possibility that differentiable neurobiological systems underlie learning (acquisition) and memory (retention and/or retrieval) are discussed. Experiment two attempted to generalize the contrasting effects of a single dosage schedule of the drug to an aversively motivated successive reversal learning task, but the effort did not succeed. (Journal abstract modified)

193582 Liebman, Jeffrey Mark. University of California, Los Angeles **A pharmacological and neuroanatomical analysis of dopaminergic and noradrenergic pathways involved in self-stimulation in rats. (Ph. D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-32070 HC$12.50 MF$4.00 150 p.

The sensitivity of self-stimulation in lateral hypothalamus and mesencephalic central gray matter to manipulations of dopaminergic, as well as noradrenergic, neurotransmission was investigated in rats. A bar pressing task was used, and results indicated that neurotransmitter systems containing dopamine are critical for self-stimulation. The possibility remained, however, that these effects were mediated by indirect effects of dopamine containing structures, particularly corpus striatum, on SS in nondopaminergic substrates. An experimental paradigm was used to evaluate this possibility which used pharmacological agents influencing dopaminergic and noradrenergic neurotransmission in rats who self-stimulated in substantia nigra or in lateral hypothalamus. Pimozide, a dopamine receptor blocker, depressed SS in substantia nigra more than in lateral hypothalamus. Apomorphine at a low dose level increased SS in lateral hypothalamus while not influencing it in substantia nigra. Results are attributed to an occlusive interaction between the dopamine receptor stimulating action of apomorphine and the postsynaptic action of dopamine released by stimulation in substantia nigra. A tentative scheme of substrates of SS is proposed. (Journal abstract modified)

193745 Herr, John Jackson. University of Southern California **Differential effects of epinephrine and propranolol on shuttle box avoidance learning in rats of different ages. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-921 HC$12.50 MF$4.00 69 p.

The Eisdorfer hypothesis that performance decrements with age can be explained by the inverted U relationship between arousal and performance by assuming older Ss are overaroused was tested. The shuttle box avoidance task was used to test the hypothesis in female Simonsen Albino rats of 3.5and 9.5months of age who were injected with epinephrine, propranolol HCl or peanut oil (control). Older control Ss performed significantly better than younger controls (suggesting that the former were at a higher initial level of peripheral autonomic end organ arousal). Propranolol, which should lower peripheral autonomic end organ arousal, significantly impaired the performance of Ss of both ages. Epinephrine, which should elevate peripheral autonomic end organ arousal, significantly impaired performance of older Ss, but failed to have a significant effect on younger Ss. A subsequent replication experiment resulted in similar findings. It is concluded that the Eisdorfer hypothesis can be generalized to a different species, task, and manipulation of peripheral autonomic end organ arousal to successfully predict performance differences based on age. (Journal abstract modified)

194130 Hood, Ronald D.; Melvin, Kenneth B.; Starling, Patricia B. Univ. of Alabama, University, AL 35486 **Effects of agroclavine on avoidance behavior in the hamster.** Bulletin of the Psychonomic Society. 3(1B):71-72, 1974.

The relationship of agroclavine to avoidance learning was examined in the rat. Four groups of hamsters received 0, 2, 6, or 10mg/kg of agroclavine. The highest dosage levels severely retarded avoidance learning, whereas the 2mg/kg group showed no decrement in learning. Gnawing was prevalent in the 6 and 10mg/kg groups. 7 references. (Author abstract modified)

194133 Calhoun, William H. Univ. of Tennessee, Knoxville, TN 37916 **Methamphetamine's effect on SDR: replication and extension.** Bulletin of the Psychonomic Society. 3(1B):78-80, 1974.

The effect of methamphetamine on serial discrimination reversal learning (SDR) was studied in rats. Selected doses reduced errors during acquisition of SDR with successive reversals spaced by either 24 or 48 h. Any conclusions regarding the duration of the drug effect in SDR were tentative. Results suggest that the drug had a residual effect on the performance of the animal which dissipated with time. 6 references. (Author abstract modified)

194152 Liebman, Jeffrey M.; Butcher, Larry L. Dept. of Psychology, Univ. of California, Los Angeles, CA 90024 **Effects of self-stimulation behavior of drugs influencing dopaminergic neurotransmission mechanisms.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 277(3):305-318, 1973.

Drugs preferentially influencing dopaminergic neurotransmission mechanisms were administered to rats which lever pressed to receive electrical stimulation in either the lateral hypothalamus or periaqueductal mesencephalon. The same drug effects were observed regardless of the site of electrical stimulation. Lever pressing behavior was observed at different dosages of the dopamine receptor blocking agents pimozide, apomorphine and L-DOPA, at control and doubled levels of self-stimulation current. Pharmacological effects on predominantly noradrenergic mechanisms were also studied. It is suggested that motor incapacity is not a sufficient explanation for most of the observed reductions in lever pressing rate. The integrity of central dopaminergic systems may be essential for the behavioral expression of certain motivational processes. 37 references. (Author abstract modified)

194178 Kuhn, D. M.; Greenberg, I.; Appel, J. B. University of South Carolina, Columbia, SC 29208 **Differential effects on lever choice and response rate produced by d-amphetamine.** Bulletin of the Psychonomic Society. 3(2):119-120, 1974.

The relationship between the threshold of discriminibility of amphetamine and changes in rate of responding known to be induced by the drug is examined. Six rats were trained to discriminate between 1.0mg/kg of d-amphetamine and saline using a two lever choice procedure. The threshold for amphetamine discriminability was then determined by gradually lowering the drug dose. Following a dose of 0.25mg/kg of d-amphetamine, rats responded about equally often on the saline and drug levers, but their overall response rates remained elevated well above saline rates. 5 references. (Author abstract modified)

194478 Parker, Robert B. Dept. of Pharmacology, Research and Development Div., Parke, Davis & Co., 2800 Plymouth Rd., Ann Arbor, MI 48106 **Mouse locomotor activity: effect of morphine, narcotic antagonists, and the interaction of morphine and narcotic antagonists.** Psychopharmacologia (Berlin). 38(1):15-23, 1974.

Six compounds (cyclazocine, levallorphan, diprenorphine (M-5050), nalorphine, naloxone, and naltrexone) were investigated in regard to their activity as antagonists of morphine induced locomotor activity and in regard to their ability to stimulate locomotor activity themselves. All six antagonized the effect of morphine, but only cyclazocine and levallorphan produced any significant stimulation of locomotor activity by themselves at the doses tested. This indicates that changes in mouse locomotor activity can be used successfully to monitor the interaction between morphine and narcotic antagonists and that locomotor activity studies can also be used to study the stimulant (agonist) properties of narcotic antagonists. 16 references. (Author abstract modified)

194568 Halki, John Joseph. University of Kansas **The effects of dextroamphetamine, dimethyltryptamine, lysergic acid diethylamide and tetrahydrocannabinol upon pregnancy and the offspring. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-12567 HC$12.50 MF$4.00 140 p.

The effect of specific psychopharmacological agents, dextroamphetamine (DAM), dimethyltryptamine (DMT), lysergic acid diethylamide (LSD) and tetrahydrocannabinol (THC) on gestation or gestational productivity in the rat was investigated. It was found that DMT, when administered to pregnant rats during organogenesis, results in poor reproductivity as evidenced by embryo absorption, stillborn progeny and small litter size. No gross congenital malformations were found in any of the offspring. The progeny of the female rats who were administered any substance at a specific time prior to breeding exhibited a diminished ability to learn to lever press for food reward. Progeny of mothers administered THC and those of males administered LSD exhibited a decreased ability to learn to lever press for food reward. Decreased learning of progeny cannot be attributed to drug dependent decreased motor activity. (Journal abstract modified)

194677 Leftoff, Sondra. New York University **Time-dependent, memory retrieval effects following peripheral and hippocampal treatments to increase synaptic biogenic amines. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-13352 HC$12.50 MF$4.00 174 p.

The effects of pharmacological alterations of the level of neurotransmitter activity at noradrenergic and serotinergic synapses were investigated at various times following learning of a brightness discrimination induced increases of the biogenic amines in the central nervous system result in disruption in retrievability of the escape task only when that task was normally well remembered. At other times when control animals indicated less than perfect recall of the habit, experimentally induced increases in these monoamines in the central nervous system was ineffective in further altering retrieval processes. The findings are similar for both intraperitoneal and intrahippocampal drug administration. The cholinergic model of synaptic alterations following learning could not account for this data. It was postulated that the biogenic amines function uniquely in the memory retrieval process along with the previously deduced cholinergic changes. (Journal abstract modified)

194736 Fukuda, Sachio; Iwahara, Shinkuro. Department of Psychology, Faculty of Education, Tokyo University of Education, 3-29-1, Ohtsuka, Bunkyo-ku, Tokyo 112, Japan **Dose effects of chlordiazepoxide upon habituation of open-field behavior in white rats.** Psychologia (Kyoto). 17(2):82-90, 1974.

Dose - response relationships of chlordiazepoxide upon habituation of open field behavior were studied in naive male rats. The drug - state changes (both from Saline (S) to chlordiazepoxide (D) and D to S) increased ambulation and rearing in the open field with D at 10 mg/kg, but at higher doses the same effect was found only from D to S, probably because of the drug's stronger muscle relaxant action. The same dishabituation effect was observed in terms of defecation and urination with the D to S shift but not with the reverse shift, probably because of the drug's depressant effect upon defecation and urination; in addition, the dose - response relationship failed to appear as in ambulation and rearing. Correlations between the two skeletal measures and the two autonomic measures were very low. 5 references. (Author abstract modified)

194956 Tamagnone, G. F.; Torrielli, M. V.; de Marchi, F. Research Department, Schiapparelli S.p.A., 10153 Turin, Italy **A new benzodiazepine: 1-(2-hydroxyethyl)-3-hydroxy-7-chloro-1, 3-dihydro-5-(o-fluorophenyl)-2H-1, 4-benzodiazepin-2-one.** Journal of Pharmacy and Pharmacology (London). 26(7):566-567, 1974.

Preparation of a series of new 1-hydroxyalkyl derivatives of 1,3-dihydro-2H-1, 4-benzodiazepin-2-ones bearing a 3-hydroxyl or a 4-N-oxide function is described. Experimental results with mice and rats indicate that the new compound exerts a central activity which appears to be superior to that of diazepam. Rats gave a pattern of responses similar to those seen in mice. Preliminary clinical assessment showed the drug to be active in the treatment of minor and severe anxiety and associated symptoms. 3 references.

195079 Williams, John M.; Hamilton, Leonard W.; Carlton, Peter L. Rutgers College, Van Brunswick, NJ **Pharmacological and anatomical dissociation of two types of habituation.** Journal of Comparative and Physiological Psychology. 87(4):724-732, 1974.

Pharmacological and anatomical dissociation of two types of habituation were reported in the rat. Both the exploration of a novel environment (an operant response) and the startle response (an elicited response) share certain functional characteristics; e.g.,both response measures wane as a function of exposure and show spontaneous recovery. This commonality has led to the assumption that both measures can be used as an index of a common process of habituation. In the present study, scopolamine (but not methyl scopolamine) greatly impaired habituation of exploration but had no direct effect upon habituation of startle. Medial septal lesions impaired the rate of habituation in both cases. These differential effects imply that, contrary to previous conceptualizations, the two measures of habituation do not reflect a unitary process and that anticholinergic drugs and medial septal damage do not influence the same neural substrate in terms of behavioral inhibition. 16 references. (Author abstract)

195081 Wisheart, Thomas B.; Walls, Elwood K. Department of Psychology, University of Saskatchewan, Saskatoon, Saskatchewan, S7N OWO, Canada **Reduction of stimulus-bound food consumption in the rat following amphetamine administration.** Journal of Comparative and Physiological Psychology. 87(4):741-745, 1974.

The effects of intraperitoneal administration of d-amphetamine on stimulus bound food consumption in sated rats were studied. Lateral hypothalamic stimulation which resulted in feeding was either programmed to occur at regular intervals or delivered by the animal's response (self-stimulation). Stimulus bound food intake was reduced by d-amphetamine, 3.0or 4.0mg/kg dosages being sufficient to cause almost complete anorexia. Reflexive sniffing and chewing of food and self-stimulation behaviors were unaffected. The results indicate that amphetamine selectively interacts with the adrenergic feeding system of the lateral hypothalamus to produce an inhibition of food consumption. 17 references. (Author abstract)

195087 Jacobs, B. L.; Eubanks, E. E.; Wise, W. D. Department of Psychology, Princeton University, Princeton, NJ 08540 **Effect of indolealkylamine manipulations on locomotor activity in rats.** Neuropharmacology (Oxford). 13(7):575-583, 1974.

The effect of various manipulations of the indolealkylamine system upon locomotor activity in adult male rats was investigated. 6-Fluorotryptophan, a rapidly acting tryptophan hydroxylase inhibitor, produced a small, but significant decrease in activity. Neither variations in the dietary content of L-tryptophan, nor systemic injections of L-tryptophan had any effect on activity. Pretreatment with the monoamine oxidase inhibitor, pargyline, caused L-tryptophan injections to produce a syndrome characterized by large increases in activity, tremor, rigidity, hyperreactivity, stereotyped head movements, and a general sympathetic response. Pretreatment with spiroperidol, a presumed specific dopamine receptor blocker, abolished all signs of the syndrome except for the rigidity and hyperreactivity. The noradrenergic receptor blockers, phenoxybenzamine and propranolol, had no observable effect on the syndrome. 22 references. (Author abstract)

195088 Rosen, A. J.; Freedman, P. E. Department of Psychology, University of Illinois, Chicago, IL **The effects of p-chloroamphetamine on instrumental conditioning in the rat.** Neuropharmacology (Oxford). 13(7):585-590, 1974.

The effects of p-chloroamphetamine on instrumental conditioning in the rat are reported. Hungry rats were given 60 training trials in a multiple continuous reinforcement (CRF) schedule under either drug (p-chloroamphetamine) or placebo (saline) conditions. A comparable 60 trial testing phase followed in which half of the subjects continued under the training injection conditions and the other half were switched to the alternative injection. Drugged subjects displayed slightly inferior discrimination performance in training as a result of elevated responding in extinction. No differences between groups were obtained on CRF performance. In the testing phase, extinction performance was similarly affected by both concurrent testing and prior training phase conditons. The data suggest that p-chloroamphetamine administration results in a selective disruption of responding to stimuli correlated with nonreward and that this effect tends to persist for long periods of time. The results are consonant with other reports of disinhibition resulting from brain serotonin depletion. 21 references. (Author abstract)

195089 Baskin, S. I.; Hinkamp, D. L.; Marquis, W. J.; Tilson, H. A. Department of Pharmacology, Medical College of Pennsylvania, Philadelphia, PA 19129 **Effects of taurine on psychomotor activity in the rat.** Neuropharmacology (Oxford). 13(7):591-594, 1974.

Taurine, a proposed neurotransmitter which possesses distinctive effects on psychomotor activity in rats was examined. Intraperitoneal injection of taurine causes a dose dependent depression of habituated psychomotor activity. Intraventricular administration of taurine results in a depression of psychomotor activity peaking at 20 min followed by a brief

stimulation in activity occuring at 60-70 min after infusion. Larger doses of taurine prolong the depressant effect and appear to mask the following stimulant effect. The behavioral properties observed for taurine suggest a functional role for taurine in the central nervous system. 19 references. (Author abstract)

195090 Carey, R. J.; Goodall, E. B. VA Hospital, Syracuse, NY **A conditioned taste aversion induced by alpha-methyl-p-tyrosine.** Neuropharmacology (Oxford). 13(7):595-600, 1974.

A conditioned taste aversion induced by alpha-methyl-p-tyrosine is reported. Rats treated with either four 50mg/kg or 100mg/kg injections of alpha-methyl-p-tyrosine (MPT) spaced 12 hr apart acquired an aversion to a 0.1% saccharin solution in a two bottle choice with water. Rats treated with either saline or four injections of 100mg/kg of MPT without saccharin present exhibited a complete preference for the saccharin solution. In a subsequent experiment, the saccharin aversion induced by the four 100mg/kg MPT injection procedure was found to persist after telencephalic norepinephrine had returned to normal levels. MPT was found to be a highly effective drug for inducing a taste aversion at dose levels which did not produce obvious signs of toxicity. 10 references. (Author abstract)

195113 Corcoran, Michael E.; Amit, Zalman. Kinsmen Laboratory of Neurological Research, University of British Columbia, Vancouver, British Columbia, Canada **The effects of hashish injections on feeding and drinking in rats.** Research Communications in Chemical Pathology and Pharmacology. 9(1):193-196, 1974.

The effects of hashish injections on feeding and drinking in rats were examined. Results indicate that the injections of two doses of hashish (5 and 10mg/kg) significantly depressed food intake. Water intake of rats under both ad libitum and deprivation conditions was also depressed. No behavioral tolerance to the suppressive effects of hashish injections on food or water intake were observed. An increase in the suppression of food intake with repeated doses under deprivation conditions was noted. 7 references.

195223 Houser, Vincent P.; Van Hart, Dale A. Psychotropic Drug Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **Effects of withdrawal from chronic amphetamine administration on activity levels of albino rats.** Psychological Reports. 35(1, Part 1):307-310, 1974.

To study the effects of amphetamine withdrawal on activity level, 18 albino rats were administered either saline or various dosages of d-amphetamine sulfate in activity wheel cages over a 13 week period, while food consumption and water consumption were reduced. Findings indicate that withdrawal of amphetamine led to significant elevations in baseline activity. It is suggested that amphetamine may produce long-lasting changes in the central nervous system which are reflected in elevated activity when the drug is withdrawn. 8 references. (Author abstract modified)

195226 Buckholtz, Neil S. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29401 **Shuttle-avoidance learning of mice: effects of post-trial pentylenetetrazol, strain and age.** Psychological Reports. 35(1, Part 1):319-326, 1974.

Two strains of mice (C57BL/6J and DBA/2J) of two different ages were given 20 trials per day for 6 days in a shuttle avoidance task. Pentylenetetrazol or saline was given ip after Trial 20 on days 1 to 5. Results show a marked strain difference with DBA/2J mice superior to C57BL/6J. Findings indicate that the effects of age on avoidance depend on both strain and sex. There was no observed effect of pentylenetetrazol on avoidence learning. A second experiment examined shuttle avoidance learning in C57BL/6J and DBA/2J mice of three age groups: adult, aged, and senile. Findings indicate that overall, DBA/2J mice performed better than C57BL/6J mice. Results reveal no deterioration in avoidance learning with increased age. 28 references. (Author abstract modified)

195231 Nurimoto, Seiichi; Ogawa, Nobuya; Ueki, Showa. Biological Research Lab., Tanabe Seiyaku Co., Ltd., Osaka, Japan **Effects of psychotropic drugs on hyperemotionality of rats with bilateral ablations of the olfactory bulbs and olfactory tubercles.** Japanese Journal of Pharmacology (Kyoto). 24(2):185-193, 1974.

The effects of psychotropic drugs on hyperemotionality of the rat with lesions in the olfactory system, including the olfactory bulbs and olfactorys (O.B.-OT. rat), were investigated, and compared with the neurotoxic effects of these drugs measured on rotarod performance of the mice with bilateral olfactory bulb ablations (O.B. mice). Chlorpromazine, reserpine and meprobamate inhibited the hyperemotionality at doses close to their neurotoxic level. Pentobarbital showed only a slight effect on the hyperemotionality at subhypnotic doses. Chlordiazepoxide, diazepam and haloperidol markedly inhibited the hyperemotionality at lower doses without causing neurotoxicity. Imipramine and amitriptyline selectively inhibited mouse killing behavior (muricide) of the O.B.-OT. rat without affecting the other hyperemotional responses to various stimuli, thus differing from tranquilizers. The mode of action of these drugs in the O.B.-OT. rat was essentially the same as observed in either the O.B. and the Septal rats. For evaluating the effects of psychotropic drugs, the O.B.-O.T. rats are superior to the O.B. and septal rats, as they share both offensive aggression of the O.B. rat and hyperreactivity of the septal rat, and furthermore they exhibited muricide in a much higher incidence soon after the brain lesions. 25 references. (Author abstract)

195294 Houser, Vincent P.; Van Hart, Dale A. Psychotropic Drug Laboratory, VA Hospital, Perry Point, MD 21902 **The effect of chlorpromazine and imipramine on the aversive threshold of rats.** Physiological Psychology. 2(3A):333-336, 1974.

The analgesic potency of chlorpromazine and imipramine in the rat was assessed, using the spatial preference technique. Chlorpromazine was able to raise the aversive threshold in a dose dependent manner in doses at or above 2.0mg/kg. These same dosages, however, also significantly reduce the number of motor responses made during threshold testing. These results were interpreted to suggest that chlorpromazine produces analgesia and/or inhibits the execution of the escape response. Imipramine, on the other hand, significantly raised the aversive threshold without reducing motor activity. These results were interpreted to suggest that imipramine produced an analgesic effect. 20 references. (Author abstract)

195305 Milner, Joel S. Dept. of Psychology, Western Carolina Univ., Cullowhee, NC 28723 **Effects of d-amphetamine on acquisition of leverpress Sidman avoidance in rats.** Physiological Psychology. 2(3A):392-396, 1974.

The effects of d-amphetamine on acquisition of lever press Sidman avoidance was studied in rats. Following intraperitoneal injections of d-amphetamine, male and female

rats showed no drug dose effects on response rates during the acquisition of a Sidman avoidance task. Dose dependent differences in shock avoidance rates were observed. Low test doses showed no effect on, moderate test doses facilitated, and high test doses inhibited shock avoidance rates. Interresponse times (IRT) indicated that females, relative to males, emitted a greater number of well timed responses and were facilitated by a relatively wider range of test doses. IRTs obtained during the acquisition study and data obtained from a motility experiment indicated that some mechanism other than increased motor activity, such as improved timing, is involved in amphetamine's facilitation of shock avoidance rates. 24 references. (Author abstract)

195430 Banerjee, Utpal. Department of Pharmacology, Faculty of Medicine, University of Malaya, Kuala Lumpur 22 -- 11, Malaysia **Programmed self-administration of potentially addictive drugs in young rats and its effects on learning.** Psychopharmacologia (Berlin). 38(2):111-124, 1974.

The effects of self-administration of potentially addictive drugs in young rats on learning were studied. Young Norwegian rats of both sexes were trained in a conditioned avoidance (CAR) or a maze learning paradigm, under the chronic influence of nine potentially addictive drugs, administered in drinking water in a step up dosage schedule. Growth of these rats was variably impeded by all drugs except ethanol and meprobamate (MPB). Compared to the water controls, acquisition of CAR was accelerated by amphetamine (AMP) and medazepam (MZP), significantly delayed by morphine and pentobarbitone (PNB), and marginally affected by ethanol, phenobarbitone (PHB), flurazepam (FZP), nitrazepam (NZP) and MPB. Except for AMP, PHB and MPB, performance generally improved upon withdrawal of the drugs. In the Y-maze experiment, the rate of maze learning was generally impeded by all drugs relative to that of the water controls. 40 references. (Author abstract modified)

195431 Frankenheim, Jerry M. Department of Pharmacology, University of Western Australia, Nedlands, Western Australia, 6009 **Effects of repeated doses of 1-delta8-trans-tetrahydrocannabinol on schedule-controlled temporally spaced responding of rats.** Psychopharmacologia (Berlin). 38(2):125-144, 1974.

The effects have been observed of chronic daily intraperitoneal injections of a marihuana (cannabis) constituent, delta8-tetrahydrocannabinol (THC), on the temporally spaced lever pressing of rats maintained under a DRL (differential reinforcement of low rates of responding) schedule of water reinforcement. A different chronic dose was given to each of four rats. During the test session following the first drug injection, the two rats which received the lower doses showed lengthy periods of no lever pressing, and the two rats receiving the higher doses showed almost no lever pressing. In the case of the lower doses, the response rate between the long pauses was increased. With repeated injections, tolerance developed to the drug induced cessation of responding at all dose levels, but increased sensitivity to the response rate increasing effect was observed. These behavioral effects were probably not mediated by drug induced changes in body temperature regulation. 54 references. (Author abstract modified)

195433 Sanger, D. J.; Key, Marilyn; Blackman, D. E. Department of Psychology, University of Birmingham, P. O. Box 363, Birmingham B 15 2 TT, England **Differential effects of chlordiazepoxide and d-amphetamine on responding maintained by a DRL schedule of reinforcement.** Psychopharmacologia (Berlin). 38(2):159-171, 1974.

The differential effects of chlordiazepoxide and d-amphetamine on responding maintained by a differential reinforcement of low rate (DRL) schedule of reinforcement were examined. Rats pressed a lever and obtained food pellets on a schedule of differential reinforcement of low rate (DRL) which required that responses were spaced at least 15 sec apart in order for them to produce reinforcement. When responding had stabilized at slow and steady rates the effects of d-amphetamine and chlordiazepoxide were assessed. Low doses of both drugs increased response rates while higher doses decreased them. Reinforcement frequency showed a dose related decrease after both drugs. When interresponse times (IRTs) were analyzed it was found that both drugs shifted the peak of the distribution towards shorter IRTs but that chlordiazepoxide also produced a specific increase in the percentage of responses after very short IRTs (bursts). When IRTs were divided into those following a reinforced response (hit) and those following a nonreinforced response (miss) it was found that bursts normally followed only misses and chlordiazepoxide consistently increased the number of bursts following misses only. Amphetamine did not affect bursts in any consistent way. 24 references. (Author abstract)

195434 Vetulani, Jerzy; Reichenberg, Krystyna; Wiszniowska, Grazyna. Department of Pharmacology, Vanderbilt University School of Medicne, T.N.I., Nashville, TN 32717 **The ineffectiveness of desipramine pretreatment on behavioral effects of 6-hydroxydopamine in nialamide-pretreated rats.** Psychopharmacologia (Berlin). 38(2):173-180, 1974.

The ineffectiveness of desipramine pretreatment on behavioral effects of 6-hydroxydopamine in nialamide pretreated rats was examined. Nonanesthetized rats, pretreated with nialamide were injected with 6-hydroxydopamine into both lateral brain ventricles. Some rats received desipramine 1 h before 6-hydroxydopamine. 6-Hydroxydopamine increased the locomotor activity and produced behavioral stimulation lasting for several hours. On the following days the open field performance of the rats receiving 6-hydroxydopamine was markedly depressed. Approximately one half of the rats receiving 6-hydroxydopamine died between day 3 and day 10 after the injection. Desipramine pretreatment did not affect the behavioral changes or mortality produced by 6-hydroxydopamine, although it counteracted the depletion of brain noradrenaline brought about by 6-hydroxydopamine. It is concluded that the behavioral changes observed after 6-hydroxydopamine injection in nialamide pretreated rats are related to the action of 6-hydroxydopamine on dopamine, and not on noradrenaline neurons. 31 references. (Author abstract)

195452 Butcher, Larry L.; Dietrich, Anthony P. Department of Psychology, University of California, 405 Hilgard Ave., Los Angeles, CA 90024 **Effects on shock-elicited aggression in mice of preferentially protecting brain monoamines against the depleting action of reserpine.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 277(1):61-70, 1973.

Drug regimes designed to preferentially prevent reserpine induced depletion of either catecholamines or 5-hydroxytryptamine (5-HT) in the brain were used to study shock elicited aggression in mice. With a drug schedule known to maintain dopamine (DA) and noradrenaline (NA) at normal levels but producing a reduction in brain 5-HT, mice displayed an increase in fighting but no change in either locomotor activity or shock threshold. Animals treated with either reserpine or with a drug regimen producing normal levels of 5-HT but reduced DA and NA showed a decrease in aggression and motility but

slightly elevated shock thresholds. In view of the motor impairment observed with the latter two regimens, it is suggested that, whereas catecholamines may play an important role in mediating the motor components of aggressive behavior, 5-HT may significantly contribute to the modulation of mood dependent aspects. 28 references. (Author abstract)

195492 Lockard, Joan S.; Levy, Rene H.; Uhlir, Vladimir; Farquhar, John A. Department of Neurological Surgery, University of Washington, Seattle, WA 98195 **Pharmacokinetic evaluation of anticonvulsants prior to efficacy testing exemplified by carbamazepine in epileptic monkey model.** Epilepsia (Amsterdam). 15(3):351-359, 1974.

The form and route of administration of carbamazepine were evaluated in normal monkeys and monkeys with spontaneous major seizures (after implantation of aluminum gel). Carbamazepine controlled seizures when given orally in two monkeys; dry pellets gave lower blood levels than a solution given by nasal gastric intubation. Since the biological half-life was less than 2 hours, the drug could not be tested when given chronically without a sustained release formulation. Thus, a dosing interval of 12 to 24 hours is clearly inadequate to sustain plasma levels for more than 5 hours. 15 references. (Author abstract modified)

195494 Celesia, Gastone G.; Booker, Harold E.; Sato, Susumu. Department of Neurology, University of Wisconsin Center for Health Sciences, Madison, WI 53706 **Brain and serum concentrations of diazepam in experimental epilepsy.** Epilepsia (Amsterdam). 15(3):417-425, 1974.

The effect of intravenous diazepam on cortical epileptogenic activity in cats in relation to brain and serum concentrations of the drug was studied. Acute epileptogenic activity was differentially affected by diazepam. Interictal cortical spikes at the primary and mirror foci were not inhibited even by massive doses. Focal seizures were inhibited by small doses in brain and in serum. Generalized pentylenetetrazol (Metrazol) induced seizures were preferentially suppressed by diazepam at concentrations ineffective against focal seizures. When cortical afterdischarges were continuous or nearly so, higher doses were required and suppression was shorter. This suggests that the intensity of epileptogenic discharges can be an important variable when the effectiveness of antiepileptic drugs is studied. 7 references. (Author abstract modified)

195906 Tricklebank, M. D.; Adlard, B. P. F. Department of Child Health, University of Manchester, Medical School, Oxford Road, Manchester M13 9PT, United Kingdom **Effects in the suckling rat of chronic treatment with tryptophan and a monoamine oxidase inhibitor.** Experimental Neurology. 45(1):79-93, 1974.

The effects in the suckling rat of chronic treatment with tryptophan and a monoamine oxidase inhibitor were investigated. Daily administration of L-tryptophan (try) and tranylcypromine (TCP) to developing rats from 10-22 days of age resulted in continuously elevated levels of cerebral 5-hydroxytryptamine (5-HT) throughout this period. Such chronic treatment led to disturbed exploratory behavior in an open field. At 22 days of age, mean latency to move from the center of the open field was significantly higher than controls, as was the mean locomotor activity. This apparent paradox was largely a function of individual animals showing extreme reactions, of either immobility or hyperactivity. In these respects acute try/TCP treatment at 22 days of age produced no significant disruption of behavior, despite higher levels of brain 5-HT than in chronically treated animals. This suggests that abnormal behavior at 22 days is a function of chronic drug treatment. However, these behavioral effects were reversible since they were not observed 4 weeks after termination of treatment. 29 references. (Author abstract)

195995 Howard, George S.; McHose, James H. Dept. of Psychology, Southern Illinois Univ., Carbondale, IL 62901 **The effects of sodium amobarbital on odor-based responding in rats.** Bulletin of the Psychonomic Society. 3(3A):185-186, 1974.

The effects of sodium amobarbital on odor based responding were examined in rats. Twenty four donor rats and 24 experimental rats received 64 trials in a straight runway on a double alternation cycle of reward and nonreward. The drug state of the donor Ss and the relationship of the reinforcement cycle for donor Ss to that for experimental Ss were factorially manipulated. Only the experimental Ss for which the donor and experimental S reinforcement cycles were correlated developed patterned responding and then only when donor Ss were undrugged. The results are interpreted as supportive of the notion that the basis for odor based patterning is an emotional response to frustrative nonreward. 9 references. (Author abstract modified)

196066 Tompkins, E. Crosby. Department of Pathology and Toxicology, Mead Johnson and Company, Evansville, IN **The use of the immobility reflex (animal hypnosis) as a possible procedure for detecting sedative activity.** Life Sciences (Oxford). 15(4):671-684, 1974.

The immobility reflex was induced in rabbits and the amount of electrical current necessary to interrupt this state was determined before and after drug administration. Morphine and the major tranquilizers elevated the arousal threshold over a wide dose range while the minor tranquilizers were active over a considerably narrower range. The sedative - hypnotics demonstrated approximately the same degree of activity as the minor tranquilizers but resulted in a loss of righting reflex at the higher doses. D-Amphetamine significantly lowered the arousal threshold. Imipramine, desmethylimipramine, nialamide, aspirin, diphenylhydantoin, chlorpheniramine, and diphenhydramine possessed little, if any, activity. Thus, the drug induced changes in arousal threshold in rabbits exhibiting the immobility reflex can be used to classify compounds possessing major or minor tranquilizing or sedative - hypnotic activity. 27 references. (Author abstract modified)

196206 File, Sandra E.; Pope, J. H. City of London Polytechnic Institute, Central House, Whitechapel High Street, London E1 7PF, England **Social interaction between drugged and undrugged rats.** Animal Learning & Behavior. 2(3):161-164, 1974.

Social interaction between two rats placed in a hole board apparatus was studied. The duration and frequency of active contact was higher for animals housed singly than for those housed in pairs, and for those tested with an unfamiliar rather than a familiar partner. Animals housed alone had a higher frequency and duration of passive contact, but the familiarity of the partner did not affect this measure. Chlorpromazine reduced the frequency of active contact but increased the frequency and duration of passive contact. When only one of the pair was drugged, both rats showed more frequent changes from one behavior to another, compared with pairs where both were in the same drug state. Animals housed alone showed the highest number of changes in behavior, and those tested with an unfamiliar partner showed a higher level than those tested with a familiar one. 14 references. (Author abstract)

196226 Liu, Robert K. Department of Pathology, School of Medicine, University of California, Los Angeles, CA 90024 **Hypothermic effects of marihuana, marihuana derivatives and chlorpromazine in laboratory mice.** Research Communications in Chemical Pathology and Pharmacology. 9(2):215-228, 1974.

Hypothermic effects of marihuana and certain marihuana analogs, including the synthetic compound dimethylheptylpyran, and of one other potent hypothermic agent, chlorpromazine, were studied in laboratory mice. Chlorpromazine was found to be the most effective agent in inducing hypothermia in mice, followed by marihuana extract distillate, dimethylheptylpyran, and delta8,9-tetrahydrocannabinol. Tolerance developed most rapidly with tetrahydrocannabinol (THC), followed by dimethylheptylpyran, marhiauana extract distillate and chlorpromazine. Tolerance to the hypothermic effects of chlorpromazine and marihuana derivatives can begin to develop after one dose, and is evident by the second day of drug administration. When delta9-THC and chlorpromazine are given alternately, tolerance to THC is almost complete by the second dose, even though the mouse still responds strongly to chlorpromazine on the intervening day. 24 references. (Author abstract modified)

196227 Craigmill, Arthur L.; Canafax, Daniel M.; Curtiss, Frederick R. College of Pharmacy, Washington State University, Pullman, WA 99163 **The interaction of delta9-tetrahydrocannabinol and d-amphetamine in aggregated mice.** Research Communciations in Chemical Pathology and Pharmacology. (92):229-241, 1974.

The effects of delta9-tetrahydrocannabinol (delta9-THC) pretreatment on motor activity, hyperthermia, brain levels of 3H-amphetamine and toxicity induced by d-amphetamine in aggregated mice were examined. Thirty minute pretreatment of aggregated mice with delta9-THC had no effect on toxicity or hyperthermia induced by d-amphetamine sulfate. Delta9-THC did significantly potentiate motor activity immediately after d-amphetamine sulfate, without affecting the brain level of 3H-d-amphetamine. Increasing the pretreatment time to 1 hour significantly potentiated motor activity and toxicity induced by d-amphetamine sulfate following delta9-THC, without affecting hyperthermia and accompanied by a significant reduction in brain levels of amphetamine. 14 references. (Author abstract)

196228 Dipasquale, G.; Welaj, P.; Rassaert, C. L. Department of Pharmacodynamics, Warner-Lambert Research Institute, Morris Plains, NJ **Prolonged pentobarbital sleeping time in adjuvant-induced polyarthritic rats.** Research COmmunications in Chemical Pathology and Pharmacology. 9(2):253-264, 1974.

An increased pentobarbital sleeping time (PST) was observed in adjuvant induced polyarthritic rats within 24 hours, continuing up to day 91. The intrapaw administration of Mycobacterium butyricum induced an increased PST in rats. At the earlier time intervals (day 2, 7, 14) dose related increases in PST and severity of the hindpaws were observed. On day 21 regardless of the dose of Mycobacterium butyricum the PST or hindpaw weights were equivalent. Phenylbutazone at doses up to 25mg/kg inhibited the severity of the polyarthritis but did not reverse the increased PST in polyarthritic rats. 22 references. (Author abstract)

196370 Baez, Luis A. Princeton University **The role of brain catecholamines in the anorectic response to amphetamine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-2312 HC$12.50 MF$4.00 79 p.

The role played by central catecholaminergic neurons in the inhibition of food intake caused by amphetamine was investigated in five experiments to determine if the catecholamine, dopamine, is responsible for the drug's anorectic effects. In experiment one, the anorectic effects of d-amphetamine were compared with those of p-hydroxyamphetamine, a centrally inactive metabolite. In experiment two, selective inhibition of catecholamine synthesis by alpha-methyl-para-tyrosine effectively antagonized amphetamine anorexia. Experiment three compared the anorectic potencies of the two stereoisomers of amphetamine. The influence of selective blockade of dopamine and norepinephrine receptors on amphetamine anorexia was investigated in experiments four and five. Overall results strongly indicate that amphetamine anorexia is a centrally mediated phenomenon, involving an action of this drug on both dopaminergic and noradrenergic neuron systems. (Journal abstract modified)

196409 Pusakulich, Robert Lee. University of Utah **Analysis of cue use in state dependent learning. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-4021 HC$12.50 MF$4.00 63 p.

Four experiments were conducted with rats in a Dashiell pattern water maze to determine if a drug (sodium pentobarbital) state can serve as the discriminative stimulus in state dependent learning and if drug and nondrug learning states are discrete at dissociative drug dosages. Results refute the drug stimulus control theory of state dependent learning in that the presence of a drug imposes a limitation on sensory processing that forced drugged Ss to learn different things than nondrugged Ss, rather than serving as a discriminative stimulus. It is hypothesized that the drug interferes with the capacity of an animal to integrate information across sensory modalities, and that drug and nondrug learning states are therefore behaviorally discrete. Drugged animals learn without extensive use of environmental cues, while nondrugged animals are unrestricted. Thus state dependent learning can be viewed as a special case of drug behavioral tolerance where drugged animals must regain the capacity to deal with cross-modality sensory integration or show dissociation. (Journal abstract modified)

196758 Rokyta, R.; Sobotka, P.; Chaloupka, Z.; Vencovsky, E. Department of Pathological Physiology, Medical Faculty, Charles University, Plzen, Lidicka 1, Czechoslovakia **The influence of cerebrolysine on higher nervous activity in adult rats.** Activitas Nervosa Superior (Praha). 16(2):94-95, 1974.

At the 11th Interdisciplinary Conference on the Experimental and Clinical Study of Higher Nervous Functions (Piestany, November, 1973), research was reported on the influence of cerebrolysine (CE) on higher nervous activity in adult rats. Cerebrolysine treated rats reached the conditioned reaction criterion more rapidly than other groups of rats which did not differ significantly with one another. Similar results were obtained for retention of the conditioned reaction. From the results, it is concluded that the injection itself -- probably through the medium of a nonspecific humoral reaction to stress -- improves the performance of experimental animals, and that cerebrolysine had a specific positive effect on the elaboration and fixation of a conditioned reaction, especially on the avoidance situation. 3 references.

197284 Hoffmeister, F.; Wuttke, W. Bayer AG, 56 Wuppertal 1, Postfach 130105, Germany **Negative reinforcing properties of morphine-antagonists in naive rhesus monkeys.** Naunyn-Schmiedeburg's Archives of Pharmacology (Berlin). 277(Supplement):32, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the negative reinforcing properties of morphine antagonists in naive rhesus monkeys were reported. Seven rhesus monkeys were trained to press a lever to turn off a white light which was associated with a drug infusion of 10 sec, scheduled to occur at 30 sec after the onset of the light. Each response during the light period terminated the light for a 1 min time out period (avoidance), a response during the injection terminated the injection (escape). Under this conditions the monkeys tolerated a high number of saline injections. Then saline was replaced by different unit doses of nalorphine, cyclazocine, codeine and cocaine each for six successive daily two hour sessions. The results show, that in naive rhesus monkeys the morphine antagonists nalorphine and cyclazocine have negative reinforcing properties. (Author abstract modified)

197286 Kuschinsky, K.; Hornykiewicz, O. Abteilung Biochemische Pharmakologie, Max-Planck-Institut fur experimentelle Medizin, D-3400 Gottingen, Hermann-Rein-Strasse 3, Germany **On the involvement of brain catecholamines in morphine-induced running activity in mice.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):R42, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the involvement of brain catecholamines in morphine induced running activity in mice was reported. Blockade of dopamine-beta-hydroxylase with sodium diethyldithiocarbamate (DDC) or of tyrosine hydroxylase with alpha-methyl-p-tyrosine (alpha-MT) inhibited the stimulating action of morphine on running activity completely. L-Dopa restored the effectiveness of morphine in mice pretreated with alpha-MT, but had only a weak effect in DDC-treated animals. Doses of morphine which induced locomotor activity produced a slight but statistically significant increase in striatal homovanillic acid concentration. Bilateral lesions in the head of the caudate nucleus attenuated the locomotor effect after morphine. Morphine increases dopaminergic activity in striata of mice by increasing the dopamine concentration at its receptors. Norepinephrine seems to have an important auxiliary function in the development of morphine induced locomotor activity. (Author abstract modified)

197291 Rohte, O.; Muntzing, J. Pharmakologische-toxikologische Abteilung der Fa. Johann A. Wulfing - Bauer u. Cie., 3212 Gronau (Leine), Germany **Effects of reserpine, 6-hydroxydopamine, p-chlorophenylalanine and a combination of these substances on the grooming behaviour of mice.** Naunyn-Schmiedeberg's Archives of Phar'macology (Berlin). 277(Supplement):R62, 1973.

At the 1973 meeting of the Deutschen Pharmakologischen Gesellschaft, the effects of reserpine, 6-hydroxydopamine, and p-chlorophenylalanine and a combination of these substances on the grooming behavior of mice were reported. Reserpine has been shown to markedly reduce the grooming behavior and body temperature of mice. These effects were accompanied by a profound reduction of the transmitter content of central and peripheral serotonergic and adrenergic neurons. Treatment of mice with 6-hydroxydopamine and p-chlorophenylalanine, which reduced the transmitter content to the same extent as treatment with reserpine, had no effect on the grooming behavior or on the body temperature. It is suggested that the effect of reserpine on the grooming behavior and body temperature has no relation to the reduction of the transmitter content of central and peripheral serotonergic and adrenergic neurons. (Author abstract modified)

197450 Frey, Leroy G.; Winter, J. C. Department of Pharmacology, School of Medicine, State University of New York, Buffalo, NY 14214 **Effects of p-acetyldeoxyephedrine on punished behavior in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(1):125-127, 1973.

The effect of p-acetyldeoxyephedrine (p-ADE) on punished behavior in the rat was examined. Rats were trained to press a bar for food on a multiple schedule in which one component was VI 30 (food) and the other was FR 10 (concurrent food and electric shock). The effects of p-ADE, a drug which produces a transient decrease in tissue levels of 5-hydroxytryptamine (5-HT), were then examined. It was found that the doses of p-ADE which are required to deplete 5-HT produce nonspecific suppression of operant behavior. These observations suggest that p-ADE is not suitable for the study of the effects of 5-HT depletion on operant behavior in the rat. 5 references. (Author abstract)

197454 Kulkarni, A. S.; Rahwan, R. G.; Bocknik, S. E. Department of Pharmacology, Research Center, Dow Chemical Company, Zionville, IN **Muricidal block induced by 5-hydroxytryptophan in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(2):308-313, 1973.

Muricidal block induced by 5-hydroxytryptophan (5-HTP) in the rat is reported. Male albino rats that consistently kill a mouse exhibited almost total suppression of killing behavior after intraperitoneal administration of 5-HTP at doses of 200mg/kg. At this dose thirst induced approach behavior was blocked only in 40% of the rats. Shock induced avoidance behavior was blocked in only 16% of the animals. Pretreatment of killer rats with Ro 4-4602/1, a decarboxylase inhibitor, prevented the blocking effect of 5-HTP. 10 references. (Author abstract)

197462 Lal, S.; Sourkes, T. L. Department of Psychiatry, McGill University, Montreal 112, Quebec, Canada **Ontogeny of stereotyped behaviour induced by apomorphine and amphetamine in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):171-182, 1973.

Ontogeny of stereotyped behavior (SB) induced by apomorphine and amphetamine in the rat were examined. Both amphetamine and apomorphine induce recognizable rudimentary SB consisting of intermittent licking in 2-day-old rats. Amphetamine induces a predominantly locomotor effect but, with increasing age, SB is the dominant behavioural response. Amphetamine produces a biphasic response in the maturing rat -- stimulation, sedation and then stimulation. At 12 days of age sniffing and reverse locomotion become part of the SB. By 18 days the SB resembles the adult response except for the prominence of forward locomotion. By 35 days the response is indistinguishable from that seen in the adult. The onset of SB following injection of apomorphine progressively decreases from 1 hr to a few minutes with advancing age; the termination time of SB also progressively decreases with age. At 20 days the pattern of SB is indistinguishable from the adult. 28 references. (Author abstract modified)

197470 Klingenstein, R. J.; Wallach, M. B.; Gershon, S. Department of Psychiatry, NYU Medical Center, New York, NY **A comparison of pimozide and thioridazine as antagonists of amphetamine-induced stereotyped behavior in dogs.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 203(1):67-71, 1973.

D-Amphetamine induced stereotyped behavior in dogs was investigated as a model for stimulant induced paranoid

psychoses in man. Amphetamine, was administered i.v. to healthy unrestrained dogs, and each dog's stereotyped behavior was noted. Pimozide was more effective than thioridazine in antagonizing D-amphetamine induced stereotyped behavior at 1.5hr after neuroleptic administration. Thioridazine, at 20 hr after administration, was as effective as pimozide was at 1.5hr. These experiments partially support a dopaminergic mechanism for amphetamine induced stereotyped behavior. 21 references. (Author abstract)

197481 Cheng, H. C.; Long, J. P. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52240 **Effects of d-isomers and l-amphetamine on 5-hydroxytryptamine receptors.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(1):124-131, 1973.

Contractile responses of amphetamine were studied on superfused helical strips of the dog dorsal metatarsal vein. Low dose of d-amphetamine induced a slow contractile response which was blocked by phentolamine and cocaine. These results indicated that responses of the vascular tissue to amphetamine were mediated by the release of norepinephrine from sympathetic nerve terminals. At high dose d-amphetamine induced a dual response: an immediate response which was blocked by cinanserin and a delayed response which was blocked by phentolamine and cocaine. These results indicated that the immediate response to d-amphetamine was due to its action at 5-hydroxytryptamine (5-HT) receptors while the delayed response was due to the indirect action of d-amphetamine of alpha-adrenergic receptors. l-Amphetamine acted in the same manner. d-Amphetamine had a greater effect than l-amphetamine at 5-HT receptors whereas there was no difference between d-isomers and l-isomers on alpha-adrenergic receptors. 13 references. (Author abstract)

197482 Salama, A. I.; Goldberg, M. E. Department of Pharmacodynamics, Warner-Lambert Research Institute, Morris Plains, NJ 07950 **Enhanced locomotor activity following amphetamine in mouse-killing rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(1):162-169, 1973.

The involvement of brain norepinephrine and dopamine in locomotor activity and stereotype behavior after amphetamine in the mouse killing rat was studied. The increased stereotype behavior (rearing) observed of D-amphetamine was similar in nonkiller (normal) and mouse killing (aggressive) rats. There was a much greater increase in spontaneous motor activity in the aggressive rat compared to normal rats following 3mg/kg of amphetamine. This enhanced effect on motor activity occurred with an already existing higher forebrain norepinephrine level. The higher dose of amphetamine did not further augment this elevation. There were no differences in the rate of uptake, maximal level or disappearance of the stimulant in the brain of killer and nonkiller rats following 3mg/kg of amphetamine. Locomotor activity does not appear to be correlated with either the release of norepinephrine or its neuronal uptake inhibition. 27 references. (Author abstract modified)

197483 Ayhan, I. H.; Randrup, A. Sct. Hans Mental Hospital, Department E, DK-4000 Roskilde, Denmark **Inhibitory effect of amphetamine, L-Dopa and apomorphine on morphine-induced behavioural excitation of rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 204(2):283-292, 1973.

The influence of amphetamine, L-Dopa and apomorphine on morphine induced hyperactivity was studied in rats. A small dose of morphine produced stimulation of locomotion, rearing and grooming. By combined administration, amphetamine, L-Dopa and apomorphine potentiated each other with respect to behavioral effects. In contrast, these three drugs strongly inhibited the occurrence of morphine induced behavioral excitation. These results support the idea that the mechanism of morphine induced hyperactivity differs from that of amphetamine, L-Dopa and apomorphine and stimulation of rats' behavior by morphine is probably not due to the activation of dopaminergic systems in the brain. 29 references. (Author abstract)

197490 Scheel-Kruger, J.; Jonas, W. Sct. Hans Mental Hospital, Central Laboratory, Dept. E. DK-4000 Roskilde, Denmark **Pharmacological studies on tetrabenazine-induced excited behaviour of rats pretreated with amphetamine or nialamide.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(1):47-65, 1973.

The tetrabenazine induced excited behavior of rats pretreated with amphetamine or nialamide was studied. Tetrabenazine injected 1.5h after various doses of amphetamine produced a 5-10 times potentiation of the amphetamine induced gross behavioral effects in rats: locomotion, rearing and stereotyped activities. The amphetamine - tetrabenazine excitation was shortlasting, 6-36 min dependent on the amphetamine dose. Tetrabenazine injected after cessation of the amphetamine excitation was also able to reinduce a shortlasting and typical amphetamine like stimulation lasting 12-18 min. Neuroleptic drugs with dopamine receptor blocking properties such as haloperidol, perphenazine and spiramide, produced in very small doses complete inhibition of all behavioral effects in the amphetamine - tetrabenazine reversal test, whereas the noradrenaline receptor blocking drugs aceperone and phenoxybenzamine, in very high doses, only produced partial inhibition of the locomotor and rearing activities. The results indicate that the strong potentiation effect of tetrabenazine in amphetamine pretreated rats is dependent on a tetrabenazine induced release of the catecholamines from a reserpine sensitive storage pool to an extragranular pool available for amphetamine release. 47 references. (Author abstract modified)

197499 Van Riezen, H.; Berendsen, H.; Rijk, H. Organon International B.V.; Oss, The Netherlands **Effects of psychotropic drugs on the emotional reactivity of rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 206(2):407, 1973.

A new test to assess psychoactive properties of drugs modified from the one used by Vossen (University of Nijmegen) is described. The effects of psychotropic drugs on the emotional reactivity of rats is reported. (Author abstract modified)

197572 Maj, J.; Pawlowski, L.; Palider, W. Institute of Pharmacology, Polish Academy of Sciences, Cracow, 52 Ojcowska, Poland **The influence of anticatecholaminergic agents on the behavioural effects of L-5-hydroxytryptophan.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):53, 1974.

At the 1974 Pharmacological meeting at Graz, the influence of anticatecholaminergic agents on the behavioral effects of L-5-hydroxytryptophan was reported. L-5-hydroxytryptophan (5-HTP) given to mice and rats (together with the peripheral decarboxylase inhibitor) increased the locomotor activity and induced some characteristic signs (e.g. head twitches). The locomotor activity stimulation was inhibited by the dopamine

and/or noradrenaline receptor blockers (spiroperidol, pimozide, haloperidol, chlorpromazine, thioridazine, clozapine, phenoxybenzamine). Similarly, stimulated activity induced by 5-HTP was antagonized by catecholamines or noradrenaline synthesis inhibitors. 5-HTP increased the flexor reflex of hind limb in spinal rat. This effect was abolished by noradrenaline receptor blockers (haloperidol, clozapine). The results suggest that the 5-HTP induced locomotor stimulation may be mediated via brain catecholamine. (Author abstract)

197574 Knoll, Bertha; Timar, Julia; Jona, Gabriella; Knoll, J. Department of Pharmacology, Semmelweis University of Medicine 1085, Budapest, Ulloi ut 26, Hungary **Changes in the acquisition of conditioned avoidance responses following midbrain raphe lesions in the** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):44, 1974.

At the 1974 Pharmacological meeting at Graz, changes in the acquisition of conditioned avoidance responses following midbrain raphe lesions in the rat were reported. Electrolytic lesion in the midbrain raphe system lowers forebrain serotonin concentration and facilitates the acquisition of a shuttle box conditioned avoidance response (CAR) in rat. In a one way avoidance system animals 3 weeks after lesions in the nucleus dorsalis and nucleus medianus raphis also show significant enhancement in the acquisition of CAR compared to the sham operated subjects. Para-bromo-methamphetamine (V-111) a new amphetamine derivative proved to be a compound of high selectivity on the serotonergic system. Single administration of V-111 either subcutaneously or orally releases serotonin and inhibits both unconditioned and conditioned escape response of rats. Rats subjected to a one month treatment with V-111 acquire faster conditioned avoidance responses in a one way apparatus but in a two way avoidance system proved to be significantly poorer learners than untreated ones. (Author abstract modified)

197578 Juvancz, P.; Nowaczyk, Therese. Department of Pharmacology, Semmelweis University of Medicine, 1085 Budapest VIII, Ulloi ut 26 Hungary **The effects of early alpha-methyldopa treatment on behaviour in the rat.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 284(4):37, 1974.

At the 1974 Pharmacological meeting at Graz, the effects of early alpha-methyl-dopa (MDOPA) treatment on the behavior in the rat were reported. MDOPA administration resulted a long lasting and strong deprivation of paradoxical sleep (PS). To test the hypothetical role of PS in the maturation of the central nervous system baby rats which were not isolated from their mother, were administered 250mg/kg MDOPA daily during the first 3 postnatal weeks. At 5-weeks-old the open field test revealed an increased locomotor activity. In shuttle box conditioning beginning from 41-days-old the treated animals had a higher rate of acquisition but the control ones reached the same level of performance. The whole brain content of norepinephrine, dopamine and serotonin was not affected. (Author abstract modified)

197684 Schnell, R. C.; Prosser, T. D.; Miya, T. S. Dept. of Pharmacy and Toxicology, School of Pharmacy, Purdue Univ., West Lafayette, IN 47907 **Cadmium-induced potentiation of hexobarbital sleep time in rats.** Experientia (Basel). 30(5):528-529, 1974.

The minimum effective dose of cadmium required to potentiate hexobarbital induced sleep time and the peak time for this phenomenon were studied in rats. This research was undertaken in response to investigations which have shown that cadmium pretreatment alters the pharmacological response to drugs. It was found that the minimal effective dose of cadmium acetate required to significantly prolong hexobarbital sleep time was 2mg/kg. Sleep times in all cadmium treated rats were significantly prolonged when compared to controls. The peak effect following cadmium treatment starts on day 2 and extends to day 5. Cadmium as an environmental pollutant is also discussed. 11 references.

197854 Simpson, Lance L. Department of Pharmacology, College of Physicians and Surgeons, Columbia University, 630 West 168th St., New York, NY 10032 **A study of the interaction between amphetamine and food deprivation.** Psychopharmacologia (Berlin). 38(4):279-286, 1974.

The effect of amphetamine on spontaneous motor behavior was studied in satiated and in food deprived rats. Amphetamine (1mg/kg) evoked a large increase in motor activity in satiated animals, and an even larger increase in motor activity in deprived animals. The magnitude of motor stimulation by amphetamine in deprived animals was roughly proportional to the duration of deprivation. Food deprivation by itself did not increase motor activity. Neither sympathectomy nor adrenalectomy modified the response to amphetamine or to amphetamine plus deprivation. The data suggest that food deprivation potentiates the action of amphetamine by a central rather than a peripheral mechanism. 14 references. (Author abstract)

197855 Vasquez, Beatriz J.; Overstreet, David H.; Russell, Roger W. Department of Psychobiology, University of California, Irvine, CA **Psychopharmacological evidence for increase in receptor sensitivity following chronic morphine treatment.** Psychopharmacologia (Berlin). 38(4):287-302, 1974.

The behavioral effects of cholinergic and adrenergic agents on fixed-ratio responding (FR5) were examined in control rats and in rats chronically treated with morphine (5mg/kg/day). Tolerance to the effects of morphine on total responses was observed, but not on rate of responding. Following tolerance development, the directly acting muscarinic agonist, pilocarpine, depressed the behavior of the morphine treated animals to a significnatly greater degree than that of the controls. Drugs which directly or indirectly stimulate alpha adrenergic and central dopaminergic receptors also affected the behavior of the morphine treated rats to a significantly greater degree. It is suggested that muscarinic cholinergic, alpha adrenergic, and central dopaminergic receptors become supersensitive to their respective neurotransmitters during chronic treatment with morphine. Such a change in receptor sensitivity could constitute a mechanism underlying the development of tolerance to morphine. 18 references. (Author abstract)

197859 Szekely, J. I.; Borsy, J.; Ildiko, Kiraly. Research Institute for Pharmaceutical Chemistry, H 1045 Budapest/Hungary, Szabadsagharcosok utja 47-49. **Potentiation of tetrabenazine-induced behavioural depression by imipramine on a discrete-trial avoidance escape schedule.** Psychopharmacologia (Berlin). 38(4):339-343, 1974.

The tetrabenazine - imipramine interaction was studied on a discrete trial avoidance escape schedule in rats. In a large dose, imipramine (30mg/kg i.p.)failed to antagonize the 10mg/kg s.c. tetrabenazine induced behavioral depression. Imipramine + tetrabenazine induced a statistically significant depression, while the same drugs alone (in similar dose) had no significant effect on responding. The depressant action of tetrabenazine was potentiated by imipramine pretreatment. 14 references. (Author abstract)

197863 Ellinwood, Everett H., Jr.; Balster, Robert L. Department of Psychiatry, Duke University Medical Center, Durham, NC 27710 **Rating the behavioral effects of amphetamine.** European Journal of Pharmacology (Amsterdam). 28(1):35-41, 1974.

A nine point rating scale with a highly standardized protocol for assessing the continuum behavioral effects of amphetamine (e.g. hyperactivity, stereotypy, dyskinetic - reactive effects) in rats is described. Dose response curves for d-amphetamine and l-amphetamine were obtained demonstrating a 4:1potency ratio of d to l. The capability of the rating scale to assess antagonism of d-amphetamine by pimozide suggested that this scale may be a useful quantitative measure of neuroleptic activity of drugs. 22 references. (Author abstract)

197865 Blundell, John E.; Leshem, Micah B. Psychology Department, University of Leeds, Leeds, LS2, 9JT, England **Central action of anorexic agents: effects of amphetamine and fenfluramine in rats with lateral hypothalamic lesions.** European Journal of Pharmacology (Amsterdam). 28(1):81-88, 1974.

The effects upon food intake of three dose levels of fenfluramine and amphetamine were compared in rats with bilateral or unilateral lesions of the lateral hypothalamus. Unilateral lesions produced little modulation of drug action but bilateral lesions brought about opposite effects on amphetamine and fenfluramine anorexia. At 8 weeks after operation amphetamine anorexia was significantly diminished in bilaterally lesioned animals whereas fenfluramine anorexia was significantly enhanced. Further tests carried out at 14 and 20 weeks after operation showed that amphetamine regained its anorexic potency in lesioned animals, while the enhanced potency of fenfluramine remained. The results are consistent with the belief that these two anorexics operate through quite separate sites and mechanisms of action. 21 references. (Author abstract)

197866 Ten Ham, Martijn; De Jong, Yeb. National Institute of Public Health, P. O. Box 1, Bilthoven, the Netherlands **Tolerance to the hypothermic and aggression-attenuating effect of delta8- and delta9-tetrahydrocannabinol in mice.** European Journal of Pharmacology (Amsterdam). 28(1):144-148, 1974.

The effects of repeated administration of delta8 and delta9-tetrahydrocannabinol delta9-(THC) on both temperature and aggression of isolated aggressive mice were investigated. In the first experiment delta9-THC, 10mg/kg, caused significant hypothermia and diminished aggression. Acute tolerance to the hypothermic effect developed, which could be overcome by doubling the dose. In the same mice no tolerance to the aggression inhibiting effect was seen. In the second experiment, delta8 and delta9-THC were compared. Both compounds caused a dose dependent decrease of body temperature. The effect of delta9-THC on body temperature was about 1.5times as strong as that of delta8-THC. Tolerance to the hypothermic effect appeared in 1 day for the 10mg/kg dose, and in about 3 days in the 25mg/kg group; no tolerance was seen to the aggression attenuating effect. 17 references. (Author abstract)

197929 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Specific asymmetric behaviour induced by the direct chemical stimulation of neostriatal dopaminergic mechanisms.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin) 285(1):83-98, 1974.

The role of neostriatal dopamine in the control of motor function was investigated by assessment of the asymmetric motor behavior resulting from the unilateral intracaudate administration of pharmacological and neurochemical substances. The unilateral intracaudate administration of dopamine to saline pretreated rats induced a mild contralateral asymmetry but lower doses of dopamine were ineffective. Pretreatment with haloperidol, nialamide or a combination of these two agents increased the sensitivity of caudate tissue to the dopamine effect. This enhancement was shown to be specific for the neuroleptic agents (haloperidol, clothiapine and oxypertine were effective whilst aceperone and phenoxybenzamine were relatively ineffective) and the contralateral behavior specific for dopamine (noradrenaline, RS 86, procaine, chlorpromazine, trifluphenazine, amitriptyline and protripytline were ineffective) although a contralateral asymmetry was observed following unilateral intracaudate atropine or 5-hydroxytryptamine. 26 references. (Author abstract modified)

197930 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Dopamine agonist and antagonist activities of piribedil (ET495) and its metabolites.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 285(1):71-81, 1974.

The intrastriatal injection technique was used in rats to determine whether the behavioral effects observed after peripherally administered piribedil which are attributable to dopaminergic stimulation and predictive of antiparkinson potential, are initiated by the parent compound or by a metabolite. Asymmetric behavior and stereotypy were used as indices of dopaminergic stimulation following unilateral and bilateral intrastriatal injections respectively and comparisons were made with the actions of dopamine and known dopamine agonists (apomorphine, D-amphetamine and L-amphetamine, amantadine, methylphenidate). The neostriatum was shown to be generally insensitive to the application of these agents in saline pretreated rats, responses being obtained only following the injection of large doses of dopamine, D-amphetamine, methylphenidate and S.584. These responses were enhanced in the presence of nialamide or nialamide/atropine but piribedil and its metabolites, other than S.584, were inactive. It is suggested that S.584 may represent the active component mediating the dopamine stimulant effects observed after peripherally administered piribedil. 23 references. (Author abstract modified)

197949 Johnson, A. M.; Vigouret, J. M.; Loew, D. M. Biological and Medical Research Division, Sandoz Ltd., Basle, Switzerland **CB 154 (2-bromo-alpha-ergokryptine, bromocriptin), a potential anti-Parkinson agent.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 2(Supplement):R40, 1974.

At the 1974 meeting of the German Pharmacological Society, the effects of CB 154 (2-bromo-alpha-ergokryptine, bromocriptin), a potential anti-Parkinson agent were reported. CB produced dose dependent stereotyped behavior, with predominant sniffing, whereas apomorphine (APO) stereotypy was more intense and included gnawing. d-Amphetamine (d-AM) stereotypy was of intermediate severity. Only slight activity was observed after L-DOPA. CB induced turning in rats contralateral to a chronic unilateral lesion in the substantia nigra produced by 6-hydroxy-dopamine. APO and L-DOPA also induced contralateral turning. After d-amphetamine ipsilateral turning was observed. Catalepsy induced in mice by prior administration of reserpine was antagonized by CB, APO, d-AM. In all tests, CB was particularly characterized by a slow onset and a prolonged duration of activity. The results reported support the hypothesis that CB is a central dopaminergic stimulant, and may be of value in the treatment of Parkinson's disease. (Journal abstract modified)

197952 Kreiskott, H.; Hofmann, H. P. Department of Neuropharmacology, Knoll AG, D 67 Ludwigshafen/Rh., Germany **Stimulation of a specific drive (predatory behavior) by p-chlorophenylalanine (pCPA) in the rat.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R50, 1974.

At the 1974 meeting of the German Pharmacological Society, the stimulatory effect of p-chlorophenylalanine (pCPA) was presented in selected nonbiting rats (without starvation and isolation) regarding dose and time dependence after single and repeated drug administration. After single oral application of pCPA a dose dependent stimulation of predatory behavior was found. Smaller doses given repeatedly on 3 consecutive days showed effects comparable with those after single administration of much higher doses. Both after single and repeated administration in all series of tests the effect reached its maximum not before several days and faded almost completely in the drug free after period. D-Methamphetamine HCl, investigated comparatively as a CNS stimulant, provoked no predatory behavior in a wide dose range with repeated administration on 10 consecutive days. (Journal abstract modified)

197953 Kruse, H. Farbwerke Hoechst AG, D-6230 Frankfurt/Main 80, Postfach, Germany **Neurotropic effects of thyrotropin releasing hormone (TRH).** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R51, 1974.

At the 1974 meeting of the German Pharmacological Society, thyrotropin releasing hormone (TRH) was investigated for neurotropic effects in mice. In untreated animals, TRH raises the respiratory rate and body temperature and effects eye blinking, tail erection, slight muscle vibrating and trembling of the paws. In mice adapted to cages it causes a prolonged increase of motility over controls, whereas in the hold board test it reduces gross motility and explorating activity. THR counteracts many states of experimental hypothermia e.g. by reserpine, oxotremorine, clonidine, chlorpromazine, hexobarbital, lorazepam, apomorphine, pentetrazole, etc. On the other hand it intensifies the oxotremorine tremor and evokes tremor in reserpinized mice. Given two animals treated with neuroleptics like chlorpromazine, TRH inhibits muscle relaxation and in higher doses leads to excitation and death. After pretreatment with tranquilizers (lorazepam) TRH occasions increase of muscle tone and jumping. In combination with tricyclic antidepressants (imipramine, amitriptyline, etc.)TRH evokes jumping, squeaking, salivation, finally WMA and death. (Journal abstract modified)

197987 Ahlenius, S. Department of Pharmacology, University of Goteborg, Fack, S-400 33, Goteborg 33, Sweden **Effects of L-DOPA on conditioned avoidance responding after behavioural suppression by alpha-methyltyrosine or reserpine in mice.** Neuropharmacology (Oxford). 13(8):729-739, 1974.

The effects of L-DOPA on a conditioned avoidance response (CAR) suppressed by alpha-methyltyrosine methylester hydrochloride (MT), an inhibitor of the catecholamine synthesis, or by the granular uptake storage blocking agent, reserpine, have been investigated in mice. It was found that L-DOPA in conjunction with inhibition of peripheral L-DOPA decarboxylase could restore the suppression of a CAR induced by MT. A partial antagonism of the suppression induced by reserpine was obtained by L-DOPA. CAR was investigated. It was found that the reversal by L-DOPA after reserpine but not after MT resulted in significant number of false CARs. It may be that a restoration of behavior to predrug level of performance is dependent on an intact granular function ensuring release of catecholamines by nerve impulses on administration of L-DOPA. The possibility is discussed that the behavioral excitation induced by a high dose of L-DOPA is qualitatively different from the response obtained by a low dose of L-DOPA after MT reserpine. 26 references. (Author abstract)

197995 Cox, T. Department of Psychology, University of Nottingham, Nottingham NG7 2RD, England **Effects of physostigmine on the accuracy and activity of discrimination behaviour in rats.** Neuropharmacology (Oxford). 13(8):701-705, 1974.

The effects of physostigmine on the maintenance of a position discrimination and of a visual discrimination were studied in rats. Small doses of the drug improved the accuracy of performance, but reduced the animals' level of activity. Larger doses brought about a general disruption of behavior, impairing the accuracy of performance as well as markedly reducing the animals' level of activity. The dose response curve for the accuracy measure was significantly different from that for the activity measure, and the increase in difficulty across the two discriminations was associated with a shift in the dose response curves for the first, but not the second measure. These results were interpreted as supporting suggestions that the behavioral effects of physostigmine can be explained through its action on two separate cholinergic mechanisms of response inhibition. 15 references. (Author abstract)

197996 Lowy, K.; Weiss, B.; Abood, L. G. Center for Brain Research, University of Rochester Medical Center, Rochester, NY 14642 **Influence of an anticholinergic psychotomimetic agent on behaviour in cats controlled by an auditory stimulus.** Neuropharmacology (Oxford). 13(8):707-718, 1974.

An anticholinergic psychotomimetic agent was examined for its behavioral effects on cats trained to press a lever, the location of which corresponded to one of two sound sources. The cats were trained to lick a protruding sponge in dim light which then caused the main light to turn on, and an auditory signal to be emitted from either side of a panel in the chamber. Any lever response terminated the trial. A food reward was given only if the cat pressed a lever on the same side as the sound signal. A new trial cycle began when the cat licked the sponge. A computer programme controlled the experiment, stored the experimental data, and permitted an analysis of various psychophysical parameters, such as ability to localize an auditory cue, threshold of sound intensity, rate of trial onset, and lateral tendency. Doses of N-methyl 4-piperidyl-cyclobutylphenyl glycolate (CBG) reduced the number of responses, and tended to lower the relative time spent in the light period. 14 references. (Author abstract modified)

198014 Molander, Lars; Randrup, Axel. Pharmacological Department, AB Ferrosan, S-201 10 Malmo, Sweden **Investigation of the mechanism by which L-DOPA induces gnawing in mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 34(5):312-324, 1974.

The mechanism by which L-Dopa induces gnawing in mice was examined. Stereotyped behavior including gnawing was elicited in mice by L-Dopa given after various doses of the decarboxylase inhibitor Ro 4-4602. The gnawing was estimated quantitatively. The effect of various drugs including reserpine, FLA-63, spiramide and alpha-methyltyrosine on the gnawing was studied and it is concluded that the gnawing is influenced by both dopamine and noradrenaline in the brain. The relation of noradrenergic brain mechanisms to gnawing seems to be complicated. 25 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

193417 Thompson, George R.; Fleischman, Robert W.; Rosenkrantz, Harris; Braude, Monique C. Mason Research Institute, Worcester, MA **Chronic oral toxicity of cannabinoids in monkeys.** Toxicology and Applied Pharmacology. 29(1):77, 1974.

At the Thirteenth Annual Meeting of the Society of Toxicology held in March, 1974, the toxicity produced by oral administration of delta9-tetrahydrocannabinol (delta9-THC) or a crude marihuana extract (CME) was evaluated in rhesus monkeys. High dosages were chosen to produce toxicity and not to stimulate human dosages. Both compounds produced cumulative toxicity as indicated by delayed mortalities but only moribund or deceased animals exhibited significant histopathology. Both compounds produced behavioral depression. Primary tissue changes in monkeys treated with delta9-THC included atrophy of the thymus and pancreas and hemorrhagic colitis with associated myeloid hyperplasia of the bone marrow, vacuolar nephrosis and severe serum electrolyte derangement. Delta9-THC and CME produced adrenal hyperplasis in moribund monkeys, anorexia and weight loss. Hematological and hemochemical parameters were generally unaffected. After tolerance developed, some monkeys exhibited moderate hyperactivity. (Journal abstract modified)

194483 Roberge, Andree G.; Poirier, L. J. Laboratoires de Neurobiologie, Faculte de Medecine, Universite Laval, Quebec, Canada **Brain dopa/5-HTP decarboxylase activity after the chronic administration of L-dopa or 5-hydroxy-L-tryptophan in normal and lesioned cats.** Brain Research (Amsterdam). 76(3):401-412, 1974.

The effect of chronically administered L-DOPA on DOPA/5-hydroxy-L-tryptophan (L-5-HTP) activity in cats with midbrain lesions is described. The effect of interrupting L-DOPA treatment on the time course necessary for the enzymatic activity to return to normal levels was also studied. The activity of DOPA/5-HTP decarboxylase was significantly lowered in the striatum of the lesioned side of untreated cats or cats treated with L-5-HTP. DOPA/5-HTP decarboxylase activity was significantly increased in the intact striatum of cats with a rostral tegmental lesion. No further increase was noted after chronic administration of L-DOPA. The activity of this enzyme was not significantly modified in intact striatum of untreated cats with a somewhat more caudal tegmental lesion which, however, spared the caudal hypothalamus. In the latter groups of cats, chronic treatment with L-DOPA increased DOPA/5-HTP decarboxylase activity significantly. L-5-HTP, which produced the same effect as L-DOPA on the enzymatic activity, was not the substrate allowed to generate dopamine synthesis. 44 references. (Author abstract modified)

196106 Davis, W. Marvin; Logston, David G.; Hickenbottom, John P. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Antagonism of acute amphetamine intoxication by haloperidol and propranolol.** Toxicology and Applied Pharmacology. 29(3):397-403, 1974.

The antidotal effects of a butyrophenone neuroleptic, haloperidol (HAL), and a beta-adrenergic blocking agent, propranolol HCl (PRO), against the acute toxicity of d-amphetamine sulfate (AS) were determined in rats. Both doses of PRO and of HAL afforded considerable protection against AS lethality compared to saline posttreated controls. However, th combination did not protect as well as did the more effective single agent, HAL. Hypoglycemia at 25 minutes after AS was prevented by HAL only injection at 15 minutes post-AS. The four to six fold elevation of plasma lactate at 25 minutes after AS was prevented by posttreatment with PRO but not by the HAL doses, which greatly reduced lethality. The data do not indicate that prevention of these biochemical effects of AS was critical to reduction of mortality. It is suggested that HAL and PRO deserve consideration as useful alternative or supplemental antidotes to those presently recommended for human acute intoxications from amphetamine like drugs. 23 references. (Author abstract modified)

197455 Merritt, J. H.; Medina, M. A. Forensic Toxicology Branch, USAF School of Aerospace Medicine, Brooks AFB, TX **Effect of simulated altitude on the disposition of chlorpromazine in mouse brain and liver.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 201(2):347-352, 1973.

The effect of simulated altitude on the disposition of chlorpromazine in mouse brain and liver was examined. After a single injection of 5mg/kg, accumulation of 35S-chlorpromazine was greater in the brains of mice previously exposed to 18000 ft of simulated altitude than in ground level control animals. There was no significant difference between the two groups with respect to chlorpromazine concentration in the liver. Nor was there a significant difference in the in vitro hepatic microsomal metabolism of chlorpromazine. The significance of these findings is discussed in relation to the administration of drugs to humans under altitude conditions. 16 references. (Author abstract)

197815 Bazemore, Robert P.; Zuckermann, Emil C. Dept. of Neurology, Yale Univ. School of Medicine, 333 Cedar St., New Haven, CT 06510 **On the problem of diphenylhydantoin-induced seizures: an experimental approach.** Archives of Neurology. 31(4):243-249, 1974.

The response of animals to the long-term and short-term administration of toxic doses of diphenylhydantoin was evaluated while they were monitored electroencephalographically for evidence of seizure activity or of any change in the electroconvulsive threshold. During acute and chronic diphenylhydantoin intoxication, seizure like episodes, observed clinically by others, were not accompanied by any electroencephalographic evidence of seizure activity. The electroconvulsive threshold rose during the development of acute diphenylhydantoin intoxication and was maintained at high levels during chronic intoxication. Diphenylhydantoin did not worsen pentylenetetrazol induced seizures but tended to protect against them. 50 references. (Author abstract modified)

06 METHODS DEVELOPMENT

197967 Niemeyer, D. H.; Krieglstein, J. Department of Pharmacology, University of Mainz, D-6500 Mainz, Obere Zahlbacherstrasse 67, Germany **Determination of noradrenaline, dopamine, serotonin, 5-hydroxyindoleacetic acid, tyrosine and tryptophane in the isolated perfused rat brain.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R71, 1974.

At the 1974 meeting of the German Pharmacological Society, the suitability of the isolated perfused rat brain for monoamine research was reported. After 30 min of perfusion of the isolated rat brain, noradrenaline (NA), dopamine (DA), serotonin (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), tyrosine (Tyr) and typtophane (TP) were separated and determined fluorometrically. Compared to rat brains in vivo, there was no change in the content of DA, 5-HT, Tyr and TP; NA decreased by 17% and 5-HIAA increased by 21%. The concen-

tration of Tyr and TP in brain increased two and four fold respectively after perfusion with Tyr and TP; only 5-HT increased by 40% whereas the other substances studied remained unchanged. Addition of reserpine to the perfusion medium led to the expected decrease of NA, DA and 5-HT and to an increase of 5-HIAA. It is concluded that the isolated perfused rat brain is comparable to rat brain in vivo and is suitable for monoamine studies. (Journal abstract modified)

198056 Randall, Lowell O. Department of Pharmacology, Hoffman-La Roche, Inc., Nutley, NJ **The screening of benzodiazepines.** Psychopharmacology Bulletin. 10(2):22-23, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which described the separation of the benzodiazepines from the hypnotics and tranquilizers by specific animal tests. It was reported that benzodiazepines and their analogs may be separated into low, moderate, and high potency groups, which show a satisfactory correlation between human and animal trials. Differentiation of benzodiazepines (chlorpromazine) and barbiturates (pentobarbital, amobarbital) in various animal trials were reported. 11 references. (Journal abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

196674 Ayd, Frank J., Jr. Taylor Manor Hospital, Ellicott City, MD 21043 **A critical evaluation of molindone (Moban): a new indole derivative neuroleptic.** Diseases of the Nervous System. 35(10):447-452, 1974.

An evaluation of molindone (Moban), a new indole derivative neuroleptic, is presented. Data gathered from a 9 year clinical experience verified that it is an antipsychotic drug comparable with respect to efficacy and safety to the established neuroleptics. The technique of therapy, the safety, long-term therapy, overdosage and interaction with other drugs is discussed. Like the piperazine phenothiazines, Moban caused fewer side-effects, except extrapyramidal reactions, than the piperidine and aliphatic derivatives. It is not as potent as trifluoperazine, fluphenazine, haloperidol and thiothixene, so a somewhat higher milligram dose may be required to achieve the same therapeutic response. 31 references. (Author abstract modified)

196675 Small, Joyce G.; Kellams, Jeffrey. Larue D. Carter Memorial Hospital, Dept. of Psychiatry, Indiana Univ. School of Medicine, 1315 West Tenth St., Indianapolis, IN 46202 **Early hospital experiences with fluphenazine decanoate.** Diseases of the Nervous System. 35(10):453-456, 1974.

Data are reported concerning the first year of hospital use of fluphenazine decanoate. Observations reveal that staff psychiatrists were cautious in their initial use of this product, consistently reserving it for those patients who were very uncooperative about taking oral medications. Outcome of treatment was regarded as satisfactory in only 38% of the patients and a number of unusually severe and prolonged side-effects were encountered. A conservative position about the use of depot medications in the treatment of schizophrenia is advocated until further studies of specific target areas for such treatment can be accomplished. 23 references. (Author abstract)

196678 Prien, Robert F.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Laboratory, VA Hospital, Perry Point, MD **The current status of lithium prophylaxis.** Diseases of the Nervous System. 35(10)):470-471, 1974.

The current status of lithium prophylaxis is examined. Results from controlled trials indicate that: lithium is more effective than placebo in both bipolar and unipolar illness; lithium is more effective than imipramine in bipolar illness; lithium and imipramine are equally effective in unipolar illness. Lithium is reported to be more effective than placebo in preventing both manic and depressive episodes and more effective than imipramine in preventing manic episodes. There is no reported difference between lithium and imipramine in the prevention of depressive episodes. The term prophylaxis is defined and it is stressed that lithium is not a panacea. 18 references. (Author abstract modified)

196704 Prasadio, Triman; Maramis, W. F. Department of Psychiatry, Faculty of Medicine, Airlangga University, Surabaya, Indonesia **The effects of Pabenol Complex on children with learning problems.** Jiwa, Majalah Psikiatri (Indonesian Psychiatric Quarterly) (Jakarta). 6(4)95-99, 1973.

The effects of a new drug, Pabenol Complex, on Indonesian children with difficulties in concentration, memory, and apprehension are described. The drug is a combination of dimethylaminoethanol, glutamine, and calcium fructose 1,6-diphosphate. A total of 84 children from 6 to 12 years (mean, 8.9years) of age in the first, second, and third grades with poor marks in at least three different subjects were evaluated. Sixty six cchildren completed the required number of evaluations and 18 children were considered dropouts. Pabenol Complex was administered three times daily regardless of age and bodyweight and the average IQ increase was 4.0% to 4.9%. The clinical improvement was highest in memory difficulties (56.1%) and the lowest in behavior control (30.3%), with an overall improvement of 45.5%, which is 21.7% higher than the assumed placebo effect. The overall scholastic achievement was improved with 44.3% and was best for language (53.0%) and worst for writing 31.8%). No clinical side-effects were noted. 7 references. (Author abstract modified)

198041 Itil, Turan M. Dept. of Clinical Neurophysiology and Psychopharmacology, Missouri Institute of Psychiatry, Univ. of Missouri, St. Louis, MO **Report of Early Clinical Drug Evaluation Unit #11.** Psychopharmacology Bulletin. 10(2):5-7, 1974.

At the Early Clinical Drug Evaluation Unit's meeting in May 1973, a paper was presented which reported the results of qualitative pharmaco-EEG and clinical pharmacology trials on normal volunteers after a single oral dose. Computerized cerebral biopotentials were studied to find the answers to questions about the central nervous system effectiveness, prediction of clinical application, effective dosage ranges, and time and dose related changes in brain function for the following drugs: amoxapine, loxapine, amitriptyline, protriptyline, chlorazepate dipotassium, phenobarbital, and other tranquilizers and antidepressants. Clinical trials determined the effects of the following: thiothixene and thioridazine on chronic brain syndrome, chlorazepate dipotassium on tardive dyskinesia, and other antidepressants and tranquilizers on a variety of psychotic syndrome. (Journal abstract modified)

198043 Gallant, Donald M. Department of Psychiatry and Neurology, Tulane University School of Medicine, New Orleans, LA **Report on the Early Clinical Drug Evaluation Unit.** Psychopharmacology Bulletin. 10(2):8-9, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which described the positive results of eight studies on human subjects and 10 drug evaluation projects in animals. The following positive results were reported: molindone was found to have antipsychotic effects; loxapine was adequate in treating severely ill and chronically hospitalized schizophrenics; ORF-8063, a benzodiazepine derivative, was tested on alcoholic patients and found to have antianxiety activities, but the number of patients was too small for definitive results; patients with the symptom of alcoholism showed a statistically significant advantage with Inderal; double-blind evaluation found that amoxapine has antidepressant activities, but lacks any antianxiety properties; and penfluridol was found to be just as efficacious as haloperidol as a long-acting antipsychotic. (Journal abstract modified)

198053 Ban, T. A.; Lehmann, H. E.; Amin, M.; Galvan, L.; Nair, N. P. V.; Vergara, L.; Zoch, C. Division of Psychopharmacology, McGill University, Montreal, Quebec, Canada **Systematic clinical studies with trazodone.** Psychopharmacology Bulletin. 10(2):18-19, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which reported the psychoactive properties of trazodone. A systematic clinical study in three stages was reported, aimed at revealing the range of the therapeutic properties of trazodone in psychoneuroses, depression, schizophrenia and organic brain syndrome, with and without controls, and establishing the comparative efficacy of trazodone and other approved psychoactive agents. 1 reference. (Journal abstract modified)

198060 Fink, Max. Department of Psychiatry, Health Sciences Center, State University of New York, Stony Brook, NY **EEG profiles as predictors of psychotropic drug classification.** Psychopharmacology Bulletin. 10(2):27-29, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which focused on single dose studies in alert, normal male volunteers, using multiple doses to define dose - response patterns. EEG signals were reduced by power spectral density and by baseline cross or first derivative period analysis. The final comparisons with placebo and standards were based on distance function measures or correlation matrices. In no instance are the clinical data inconsistent with the EEG classification. 2 references. (Journal abstract modified)

198061 Campbell, Magda. New York University Medical Center, New York, NY **Children's psychopharmacology unit.** Psychopharmacology Bulletin. 10(2):45-46, 1974.

Various forms of drug therapy for use with disturbed children are being evaluated. Children with diagnoses ranging from neuroses to the most severe forms of schizophrenic disorder are tested with new drugs for toxic signs and therapeutic effectiveness at gradually increasing dose levels. A controlled study of chlorpromazine, diphenhydramine (Benadryl), and a placebo shows that the improvement of less disturbed children depends more on such factors as hospitalization, psychotherapy, and/or special education than on drugs alone. Chlorpromazine was most effective in children with more severe disorders and Benadryl was effective only in disturbed children under 10 years old. (Journal abstract modified)

198062 Cole, Jonathan O. Department of Psychiatry, Temple University, Philadelphia, PA **Early Clinical Drug Evaluation Unit.** Psychopharmacology Bulletin. 10(2):46, 1974.

The effects of various drugs on psychiatric disorders are described. Ss are acute and chronic psychiatric patients, geriatric patients, and outpatients of the Early Clinical Drug Evaluation Unit of Boston State Hospital. Thiothixene (Navane) brought about greater improvement than trifluoperazine (Stelazine) on rating scale scores as well as on measures of social and work adjustment. Patients in the Community Crisis Intervention Service and on chronic inpatient wards showed a 70% improvement rate from injected fluphenazine enanthate as compared with a 30% improvement rate of oral medication with the same drug. Diazepam (Valium) was found ineffective in the control of convulsive disorders. Comprehensive results on new drugs are provided at the Evaluation Unit through data from the Brief Psychiatric Rating Scale and the Nurses Observation Scale for Inpatient Evaluation. (Journal abstract modified)

198063 Engelhardt, David M. SUNY-Downstate Medical Center, Brooklyn, NY **Outpatient pediatric psychopharmacology.** Psychopharmacology Bulletin. 10(2):46-47, 1974.

The full range of FDA approved psychotropic drugs are being tested for their effects on children, in order to set up comprehensive guidelines for clinical drug trials on children. Autistic and hyperactive children between 4 and 12 years of age are the subjects. Each subject receives a thorough examination and then each drug is tested on 4 or 10 subjects to determine its safety and effectiveness for 3 months. If approved, the drug undergoes 3 to 12 months of trials on 10 to 20 Ss to develop dosage guidelines and is then systematically compared to other compounds. (Journal abstract modified)

198064 Gallant, Donald M. Tulane University, New Orleans, LA **Clinical evaluation of new chemotherapeutic agents.** Psychopharmacology Bulletin. 10(2):47, 1974.

New psychoactive drugs are evaluated for their effectiveness in the clinical treatment of various types of mental illness. Acute and chronic schizophrenic patients in state mental hospitals and outpatients, including alcoholics, depressives, and neurotics are studied. Drugs tested include: clopenthixol (sordinol), thiothixene, an acridane compound, haloperidol, trifluoperidol, chlorpromazine, propericiazine, metronidazole, loxapine, metiapine, diazepam, and other antipsychotics and antidepressants. (Journal abstract modified)

198065 Gershon, Samuel. New York University, New York, NY **Controlled drug evaluations.** Psychopharmacology Bulletin. 10(2):47-48, 1974.

Therapeutic effects of psychotropic drugs are evaluated and information is gathered about the full range of their pharmacological action in the laboratory, clinic, and hospital. Schizophrenic, depressed, manic-depressive and schizo-affective patients, and drug abusers serve as subjects in clinical tests, and dogs, mice, and rats are used in laboratory studies. Findings demonstrate: that lithium is effective in alleviating the manic phase of manic-depressive psychosis; that lithium treatment of schizo-affective patients may increase organic brain syndrome; that no Negro patients exhibited manic-depressive symptoms; that butaperazine is less effective than chlorpromazine and loxapine is equally effective to chlorpromazine, but has negative side-effects; that lithium may also have negative side-effects; that amphetamine psychosis is often indistinguishable from paranoid schizophrenia; that drug abusers are characterized by presence of preexisting psychiatric disturbance. (Journal (Journal abstract modified)

198066 Hollister, Leo E. Standford University, Stanford, CA **Cooperative clinical screening of psychotropic drugs.** Psychopharmacology Bulletin. 10(2):48-49, 1974.

Antipsychotic and antidepressant drugs are screened to determine their therapeutic value for depressed and newly admitted schizophrenic patients. Patient response to a wide range of dosage levels is observed and recorded by skilled clinicians and a number of standard evaluation measures are used. Drugs studied include: chlorpromazine, an acridan derivative SKF 14336, haloperidol, thiopropazate, acetophenazine, perphenazine, benzquinamide, diazepam, amitriptyline, imipramine, thioridazine, triperidol, desipramine, atropine, and oxypertine. (Journal abstract modified)

198067 Lehmann, Heinz E. Douglas Hospital, Verdun, Quebec, Canada **Comprehensive clinical studies of psychoactive drugs.** Psychopharmacology Bulletin. 10(2):49, 1974.

New psychoactive drugs are evaluated for their effectiveness in various types of mental illness. Several hundred depressives, schizophrenics, alcoholics, and other mental

hospital patients and normal individuals serve as subjects. The effectiveness of each drug is measured on various behavioral, perceptual, mental alertness, and biochemical criteria, of patients with different diagnoses. Approximately 40 different agents have been tested, including: alpha-methylbenzlhydrazine, metronidazole, carbamazepine, chlorpromazine, nortriptyline, diazepam, phenobarbitone, ethchlorvynol, blutethimide, thioproperazine, cloperthixol, thiothixene, molindore, hydroxiyzine, caffeine citrate, and methamphetamine. (Journal abstract modified)

198068 Merlis, Sidney. Central Islip State Hospital, Central Islip, NY **NIMH-PRB Early Clinical Drug Evaluation Unit.** Psychopharmacology Bulletin. 10(2):49-50, 1974.

New chemical agents were evaluated for their effectiveness in the treatment of various types of mental illness. Mental patients, including schizophrenics and depressives, and normal humans were subjects. After initial screening of 35 new drugs 15 without untoward side-effects were subjected to full scale definitive studies lasting 4 to 8 weeks. Representative drugs studied include: fluanisone (haloanisone), benzquinamide, hydroxy phenamate (Listica), LAIV, phenalkylamine (indriamide), acetophenazine, pargyline, L-DOPA, trihexyphenidyl, navane (NA 0687), SKF 14336, CL 71563, and thiothixene. (Journal abstract modified)

198069 Rickels, Karl. University of Pennsylvania, Philadelphia, PA **Early drug evaluation in neurotic outpatients.** Psychopharmacology Bulletin. 10(2):50-51, 1974.

Established and relatively new psychotropic medications are evaluated in large samples of primarily anxious and depressed outpatients diverse in symptomatology, socioeconomic and other background, and treatment setting. Other research is aimed at furthering the understanding of the drug treatment process and investigation of the methodology of data analysis. Double-blind controlled trials provided clinically relevant information on the effectiveness of many anti-anxiety and antidepressant agents. Presenting illness and its history, patient background, expectational and personality attributes, and physician attitudes and treatment styles emerged as moderators of response to active agents, placebo, or both. It is expected that this research will provide a) supplemental information on psychotropic treatment of neurotics, b) a demonstration of the impact of nonspecific factors on treatment outcome and the mechanisms of this impact, c) prognostic indicators for clinicians, d) models of operation for other research groups, and e) refinements in methodology. (Journal abstract modified)

198070 Schiele, Burtrum C. University of Minnesota, Minneapolis, MN 55455 **Early Clinical Drug Evaluation Unit.** Psychopharmacology Bulletin. 10(2):51, 1974.

New psychoactive drugs are evaluated for their effectiveness in the treatment of chronic schizophrenia, acute schizophrenia, acutely depressed, anxious neurotic, and alcoholic patients. Comprehensive data are compiled on the degree of patient improvement and on side-effects of various drugs, including the following: trifluoperazine, trifluperidol, oxazepam, thioridazine, imipramine, militracen, lithium carbonate, dopenthixol, thiothixene, chlorpromazine, SKF 14436-D, haloperidol, Trilafon, Elavil, and amitriptyline. (Journal abstract modified)

198071 Shader, Richard I.; Salzman, Carl. Massachusetts Mental Health Center, Boston, MA **Drug studies in normal females, senior citizens, and in experimental groups.** Psychopharmacology Bulletin. 10(2):52, 1974.

The effects of psychotropic drugs were studied on young and elderly subjects, in men and women, in women at different stages of their menstrual cycle, in women who are or are not taking oral contraceptives, in different personality types, and in people who are or are not participants in group activities. Experimental and central subjects placebo are compared on measurements of physiology, psychomotor activity, perceptual ability, and mood. Psychoactive agents tested include the following: imipramine, diazepam, methylphenidate, chlordiazepoxide, marihuana, and LSD. (Journal abstract modified)

198073 Sugerman, A. Arthur. New Jersey Neuropsychiatric Institute, Princeton, NJ **NIMH-PRB Early Clinical Drug Evaluation Unit.** Psychopharmacology Bulletin. 10(2):53-54, 1974.

New psychoactive drugs are evaluated for their effectiveness in the treatment of various types of mental illness. Hospitalized schiozphrenics and other selected patient groups are administered certain drugs and their effectiveness is measured through observable changes in behavior, quantitative EEG, biochemical studies and side-effects. A number of drugs have been tested and have significant antipsychotic properties, including a phenothiazine (TPS-23), two thioxanthene derivatives (SKF 10812 and thiothixene), clopenthixol, two benzodiazepine derivatives (CL-71563 and P-5227), molindone, perphenazine, chlorpromazine, prazepam, AHR-1680, and pimozide. (Journal abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

194044 Lee, J. Hillary; Branchey, Marc; Haher, E. Janet; Varga, Ervin; Simpson, George M. Research Center, Rockland State Hospital, Orangeburg, NY 10962 **Once versus thrice daily thiothixene in the treatment of schizophrenic in-patients.** British Journal of Psychiatry (London). 125:73-78, 1974.

Thirty eight chronic schizophrenic inpatients participated in a double-blind crossover comparison of once daily versus thrice daily administered thiothixene. The once daily dose was given at bedtime. Results indicate that improvement in the placebo baseline occurred with both regimens although it appeared somewhat sooner with the multiple dosage regimen. Extrapyramidal side-effects were consistently more marked with the multiple dosage regimen, though the difference reached statistical significance on only a few occasions. The practical applications of these findings are discussed, particularly in terms of maintenance therapy for both inpatients and outpatients and of the possiblity of improving prescription compliance in the latter. 21 references. (Author abstract modified)

194157 Watanabe, Akiharu. Dept. of Internal Medicine, Okayama Univ. Medical School, 2-5-1 Shikata-cho, Okayama, Japan **Effect of chronic administration of centrally acting compounds on chloramphenicol metabolism in schizophrenic patients.** Pharmacology 11(4):253-256, 1974.

The effect of chronic administration of centrally acting drugs on chloramphenicol metabolism in six schizophrenic patients on long-term therapy with phenothiazine derivatives and phenobarbital was studied, and the results are compared with results from three controls and two patients with cirrhosis of the liver. A ratio of chloramphenicol glucuronate to total nitro compounds excreted in the first 2 hour urine, following the intravenous administration of the antibiotic, was found to be higher in two schizophrenic patients. The half-life of free chloramphenicol in blood was demonstrated to be much

shorter in one of the schizophrenics than was found in controls and cirrhotic patients. 11 references. (Author abstract)

194449 Katori, Itsuo. Ishizaki Hospital, Ibaragi, Japan **Use of metamin (Flupentixol) in the department of psychiatry.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(5):557-565, 1974.

The effect of metamin (Flupentixol) on schizophrenia was studied, in an experiment in which 40 patients with schizophrenia, depression, atypical psychosis and borderline psychosis were treated with this drug. Results show individual differences in the efficacy of treatment with metamin; it was effective on anxiety, tension, depression, dull emotion, loss of volition and hypoactivity, within 1 to 2 weeks after the beginning of treatment, and a daily dose of 2-4.0mg/day was most effective. Among 27 patients who were hospitalized, 13 patients achieved remission and left the hospital; no major side-effects were observed, indicating that this drug is suitable for long-term administration. 7 references.

194457 Kawahara, Ryuzo; Hisaba, Kenko; Orita, Noriko; Nakazawa, Kazuyoshi; Okuma, Teruo. Tottori University, School of Medicine, Japan **Clinical experience of the use of penfluridol (TLP-609) for the treatment of schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(3):329-339, 1974.

Clinical experience of the use of penfluridol (TLP-609) for the treatment of schizophrenia is described. Penfluridol was found effective in about half of the observed cases, but negative side-effects apparent in almost all patients outweigh therapeutic advantages. 13 references.

194460 Kato, Hideaki; Yoshimura, Go; Ito, Itsuro; Tanijiki, Takashi. Department of Neuropsychiatry, Gifu University School of Medicine, Japan **Outpatient treatment of schizophrenia by a long lasting strong tranquilizer: use of fluphenazine enanthate.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(5):551-556, 1974.

Fluphenazine enthanate was tested for its effects on schizophrenics. Of 25 patients tested, six dropped out of the study because of negative side-effects, eight maintained complete remission of symptoms, six improved noticeably, and the rest were unimproved by treatment. 14 references.

194474 Maeda, Toshio. Niigata Mental Hospital, Japan **Examination of the effects of cloxazolam by a double-blind study of mental patients before rehabilitation.** Medical Consultation and New Remedies (Tokyo). 10(12):147-153, 1973.

The effects of cloxazolam (Cl) and diazepam (Di) were compared in a double-blind test on 30 schizophrenics. After 4 weeks, 10 patients dropped out because of remission or side-effects. Cl was more effective in improving general schizophrenic symptoms than Di, and no significant difference in side-effects was observed between the two drugs except that Cl caused more insomnia and Di caused a sense of fatigue. 16 references.

194476 Hirota, Noriyasu. National Omura Hospital, Japan **Treatment of schizophrenia by the administration of a small dose of Forit for comparatively long periods of time.** Medical Consultation and New Remedies (Tokyo). 10(12):137-141, 1973.

The effect of small dose, long-term administration of Forit on schizophrenia is discussed. Six schizophrenic patients with main symptoms of hallucination, insomnia, autism, lack of volition, lack of facial expression, dull emotion, silence, soliloquy, and meaningless smile were treated with Forit for 1 to 1.5years and other psychotropic drugs. One patient showed remarkable improvement and achieved rehabilitation, three patients showed fairly good improvement and became more active in occupational and recreational therapy, one showed slight improvement and became able to passively participate in psychotherapies, and one showed no improvement. One subject developed a tic as a side-effect of treatment. 8 references.

194512 Sugano, Keiju; Yoshida, Masao; Suzuki, Shinsuke; Sato, Chikaji; Takakosu, Yoshihide; Ichihashi, Hideo. Koriyama Mental Hospital, Japan **Use of sulpiride in the treatment of schizophrenia.** Medical Consultation and New Remedies (Tokyo). 10(11):231-249, 1973.

The effect of sulpiride on schizophrenics was studied, based on an experiment with 61 patients, 59 of whom had not responded to previous psychopharmacological treatment. All but one of the acute schizophrenics showed improvement after sulpiride treatment. Among 48 chronic patients, 10 showed extreme to moderate improvement, 17 showed slight improvement, 15 showed no improvement, and six showed aggravation. Aggravation consisted of reappearance or increase in hallucinations, delusion, hyperactivity, excitation, impulsive behavior, lack of volition, and selfish behavior. Side-effects included loss of appetite, akathisia, excitation, dystonia, insomnia and tremor.

194711 Deo, V. R. Central Mental Hospital, Yerawada, Poona-6, India **Tranquillizing action of a crystalline fraction of Paspalum scrobiculatum extract in fourteen psychotic patients.** Indian Journal of Medical Sciences (Bombay). 25(6):389-391, 1971.

A crystalline fraction BZ5 obtained from the dried alcoholic extract of the seeds of Paspalum scrobiculatum was administered orally to 14 acutely agitated psychotic patients of whom 11 suffered from schizophrenia. Crystalline BZ5 produced tranquility and other beneficial effects in nine schizophrenic patients. Signs of Parkinsonism were not noticed, but reversible hypotension was seen in three patients. Like the dried alcoholic extract crystalline BZ5 produced its beneficial effects only in schizophrenic patients. 9 references. (Author abstract)

194860 Claghorn, James L.; Johnstone, Edwin E.; Cook, Thomas H.; Itschner, Lorri. Texas Research Institute of Mental Sciences, Texas Medical Center, 1300 Moursand Ave., Houston, TX 77025 **Group therapy and maintenance treatment of schizophrenics.** Archives of General Psychiatry. 31(3):361-365, 1974.

Group psychotherapy and antipsychotic medications were employed in the treatment of 49 outpatient schizophrenics. Two treatment regimens, using thiothixene and chlorpromazine hydrochloride, were divided into group therapy and nongroup therapy subgroups for a duration of 6 months. Patients' symptoms were evaluated on a monthly basis through use of a physician's global assessment, and the Brief Psychiatric Rating Scale. Subtle changes in subjects' interpersonal emotional adjustment (a possible positive effect of psychotherapy) were measured before and after treatment by means of the Interpersonal Test Battery. Results indicated no substantial difference between medications, but a positive change over this time period for both drug regimens. While group therapy did not alter patients' symptomatology, it did, according to projective test results, deepen the subjects' awareness and insight into their own behavior. 5 references. (Author abstract)

195115 Sankar, D. V. Siva. Division of Research, Queens Children's Hospital, Bellerose, NY 11426 **Profile-based-therapy (PBT) in schizophrenias: a preclinical indication for the use of dihydroxyphenylserine (DOPS).** Research Communications in Chemical Pathology and Pharmacology. 9(1):79-83, 1974.

Profile based therapy in schizophrenias is discussed. Schizophrenia has eluded the challenge of biological investigations because of the probable multiplicity of etiological and pathobiological factors. In view of this it is suggested that a profile of biological and clinical factors should be worked out for each patient, and a particular defect should be treated on an individual profile basis in any given case. It has been shown that there is lower uptake of serotonin by thrombocytes in autistic(schizophrenic) children. One possible therapeutic drug in these cases may be dihydroxyphenylserine, alone or in combination with lithium carbonate, as it is able to increase serotonin uptake by rabbit platelets in laboratory studies. 6 references. (Author abstract)

195615 Kishore, Baldev; Dhillon, A. K. Punjab Medical Hospital, Amritsar, India **Clinical efficacy of pimozide in hospitalised chronic schizophrenics.** Indian Journal of Psychiatry (Madurai). 15(4):311-318, 1973.

The advantages and efficacy of Pimozide in hospitalized chronic schizophrenic patients who might relapse without neuroleptic maintenance are assessed. Optimal dosage for 40 female patients over a 3 month is calculated. Amelioration in psychotic symptoms and low toxicity is noted, with a 70% improvement rate. It is concluded that Pimozide is safer and more effective than chlorpromazine or prochlorperazine. Improvements in disorientation symptoms are also reported. 6 references. (Author abstract modified)

196069 DeSousa, Alan; Nayani, G. R. Dept. of Psychiatry, Grant Medical College, Bombay, India **A controlled trial of trifluperidol with trifluoperazine.** Indian Journal of Psychiatry (Madurai). 15(3):290-293, 1973.

The therapeutic efficacies of trifluperidol and trifluoperazine were compared in a controlled study. Ss were 50 schizophrenics selected from an outpatient department of a Bombay hospital. Results of the treatment were compared at 2 and 6 weeks. Trifluperidol controlled excitement and insomnia better than trifluoperazine which in turn controlled delusions and hallucinations better than trifluperidol. Both drugs showed comparable efficacy in controlling concentration and irrelevant talk. The side-effects such as extrapyramidal symptoms were found in both drugs. (Author abstract modified)

196088 Dasgupta, D.; Mallaya, U. L.; Rao, V. Bapuji; Gopinath, P. S.; Sardarilal. Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India **Psychosis in systemic lupus erythematosus.** Journal of the Indian Medical Association (Calcutta). 56(8):234-235, 1971.

A case of systemic lupus erythematosus with a schizophrenic type of psychosis is described, and a brief review of the literature is included. The patient described in the case study had butterfly skin lesion, typical skin histopathology and psychosis as major criteria along with hepatomegaly, alopecia, unexplained fever and anemia as minor criteria. The patient was first presented as pure depressive without any psychotic features but later developed a psychotic reaction, which appeared to be schizophrenic and not an organic confusional state. The psychosis was successfully treated with prednisolone, chlorpromazine, and electroconvulsive therapy. 10 references. (Author abstract modified)

196144 Koshino, Yoshifumi; Enokido, Hideaki; Matsumoto, Kanji; Matsuoka, Toshisato; Nakagawa, Fusako; Otsuka, Ryosaku. Department of Neuropsychiatry, Kanazawa University School of Medicine, Japan **Serial EEG recordings in psychotropic drug treatment.** Clinical Psychiatry (Tokyo). 16(4):387-396, 1974.

EEG changes in five schizophrenic patients during psychotropic treatment are discussed. The patients had serious pathological experience and excitation and were treated with levomepromazine (LP). Although they had no EEG abnormality before LP treatment, they all showed EEG abnormality immediately after the beginning of LP treatment. Among three patients whose LP treatment was terminated, two resumed normal EEG 2 to 3 weeks after termination of LP, and the other showed more abnormality 4 to 10 days after termination of LP than during LP treatment, but his EEG gradually resumed normal level 16 days after LP treatment. 40 references.

196601 Goldberg, Harold L.; DiMascio, Alberto. West-Ros-Park Mental Health Center, Boston State Hospital, Boston, MA **Diagnosing and treating chronic schizophrenia.** Hospital Physician. 10(10):48-49, 52, 57-59, 62, 67, 1974.

Diagnosis and psychotherapy for schizophrenia are reviewed. Symptoms are divided into those that are a result of long-term hospitalization and those not a result of having been institutionalized; hospitalization induced symptoms include motivational decline. Seven hints on long-term drug therapy are included and several classes of marketed antipsychotics are listed. Maintenance dosage and some of the hazards of long-term medication are outlined. Rehabilitation and possible acculturation are also discussed. 3 references.

196707 Bagadia, V. N.; Ghadiali, H. N.; Pradhan, P. V.; Shah, L. P. King Edward's Memorial Hospital, Bombay, India **Pimozide (R 6238) in schizophrenia (a pilot study).** Indian Journal of Psychiatry (Madurai). 15(4):319-324, 1973.

Treatment of 61 schizophrenic patients with the neuroleptic drug Pimozide is described. Fifty continued the treatment for the total trial period of 12 weeks. Side-effects were extrapyramidal reaction (including tremors and ridigity), nausea, and vomiting. No significant change was seen in hemogram, liver function tests, blood urea, blood sugar, and urine tests. Of the 50 cases, improvement was maintained in 62% and increased in 26% of the patients. The results suggest that thought disorders, paranoid and persecution ideas and psychomotor retardation remit in a large majority. 4 references.

197142 Weeks, P. Professorial Psychiatric Unit, Queen Elizabeth Medical Centre, Birmingham, England **Pamela -- a paranoid schizophrenic.** Nursing Times (London). 70(36):1388-1390, 1974.

A case study of a paranoid schizophrenic who, as a result of early efficient treatment, was able to resume her role in the home, as well as in society, by acquiring employment in the community is reported. Her personal and family history are discussed. She was treated with trifluperidol and benztropine, and a nurse was assigned to organize her day to day activities and to accompany her throughout most of the day. ECT treatments resulted in a substantial improvement of the patient's condition. She was given a parttime job and was eventually discharged to an outpatient clinic.

198047 Ota, K. Y.; Kurland, A. A. Spring Grove State Hospital, Maryland Psychiatric Research Center, Catonsville, MD **Safety evaluation of penfluridol.** Psychopharmacology Bulletin. 10(2):11-12, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which evaluated the effectiveness of penfluridol as a neuroleptic agent on a weekly dosage. Twelve chronic schizophrenic patients residing in a state psychiatric hospital were treated over a 17 week period, with initial dosages of penfluridol of 5 or 10mg gradually increased to a maximum dosage of 200mg. Patients requiring continued antipsychotic medication were maintained on penfluridol without any adverse reactions other than those usually associated with the administration of neuroleptics. There was a noticeable lack of the sedative effects commonly associated with phenothiazines. (Journal abstract modified)

198052 Simpson, George M. Research Center, Rockland State Hospital, Orangeburg, NY **Patterns of psychotropic drug use for schizophrenia.** Psychopharmacology Bulletin. 10(2):18, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which included a quantitative and qualitative analysis of the characteristics of patients receiving psychotropic agents in a state hospital. Females received higher amounts of neuroleptics than males, irrespective of age or diagnosis, and neuroleptics were prescribed more often than minor tranquilizers, antidepressants, or antiparkinson agents. It is concluded that this pattern represents a target symptom approach to treatment which should be corrected by educational programs. (Journal abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

193040 Cole, Jonathan O. Boston State Hospital, Boston, MA **The current status of lithium treatment.** Massachusetts Journal of Mental Health. 3(1):4-13, 1974.

Studies relating to effectiveness of lithium carbonate in treatment and prevention of affective illness are reviewed. Evidence indicates that lithium is a reasonably effective treatment for hypomanic states and for manic states under some conditions. It is probably useful in the prevention of future episodes of mania, and to a lesser extent, affective disorders in general. The need for further studies to confirm prophylactic value is indicated, and guidelines for monitoring blood levels during treatment are presented. 12 references. (Author abstract modified)

193060 Mitchell, Ross. Fulbourn Hospital, Cambridge, England **Manic depression.** Nursing Times (London). 70(31):1199-1201, 1974.

Manic depression is studied, noting traditional and modern views. Clinical features presented are endogenous depression and hypomania. A case study is cited. Modern ideas on causation include hormonal studies, electrolyte studies, and the amine hypothesis. Management techniques discussed are drug treatment, electroconvulsant therapy, and psychosurgery.

193068 Prien, Robert F.; Caffey, Eugene M., Jr.; Klett, C. James. Central Neuropsychiatric Research Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **Factors associated with treatment success in lithium carbonate prophylaxis: report of the Veterans Administration and National Institute of Mental Health Collaborative Study Group.** Archives of General Psychiatry. 31(2):189-192, 1974.

A multihospital collaborative study evaluated prophylactic lithium carbonate therapy in 205 patients with bipolar manic-depressive illness. Factors associated with poor lithium carbonate response are the following: (1) a recent history of frequent affective episodes requiring hospitalization, and (2) previous failure of lithium carbonate treatment. Results also suggest that lithium carbonate response may be related to the presence of schizoaffective illness and a family history of bipolar affective illness, but the small numbers of patients in these groups limit interpretation. Most failures on lithium carbonate therapy occur during the first year. Ability to remain on the maintenance schedule with no episodes for a year may be the most potent predictor of ultimate prophylactic success. There are important implications in these findings for the clinician selecting patients for prophylactic treatment. 22 references. (Author abstract)

194071 Romagnoli, Cesare; Bardin, Piergiorgio; Gastaldo, Giovanni; Merlini, Luciano. Ospedale Civile, 'S. Maria Ca' Cafoncello', D. Treviso, Italy **/Small doses of sulpiride in the treatment of psychoneurotic syndromes./** Le 'picole' dosi di sulpiride nel trattamento delle sindromi psiconevrotiche. Rivista di Psichiatria (Roma). 7(5):389-397, 1974.

The effects os sulpiride treatment administered to 34 patients suffering from psychneurotic syndromes were studied. Twenty nine of the patients were women five were men, and all were between the ages of 16 and 38. Small doses ranging from 150 to 300mg were administered daily for a period raning from 10 days to 4 months. Positive results were noticed in 80% of the patients. Tolerance was excellent and extrapyramidal disturbances were not present. It is conceded that sulpiride is advantageous in the treatment of neuropsychiatric pathology. 15 references. (Author abstract modified)

194168 Vacaflor, L.; Ananth, J. V.; Lehmann, H. E.; Ban, T. A. Douglas Hospital, 6875 Lasalle Blvd., Verdun, Quebec, Canada **Prophylactic use of lithium.** Indian Journal of Psychiatry (Madurai). 15(3):257-263, 1973.

A clinical study of an assumed prophylactic effect of lithium in recurrent affective disorders over a period of 3 years compared with that of a prior 3 year period without lithium is reported. Twenty patients suffering from recurrent affective disorders were folowed while on lithium therapy and experimental method, assessment of treatment of success, and medication are described. The findings suggest that lithium carbonate is a clinically effective prophylactic agent in the therapeutic management of recurrent affective disorders. The intensity of psychopathology observed during episodes while patients were on lithium was also reduced. Findings support the research of others. 14 references. (Author abstract modified)

194355 Prien, Robert F.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Laboratory, VA Hospital, Perry Point, MD **Lithium prophylaxis -- a critical review.** Perry Point, Md., Veterans Administration Hospital, August, 1974. 11 p.

The question of whether lithium is or is not prophylactically effective in recurrent affective illness is considered, and literature on lithium prophylaxis is reviewed, with particular emphasis on studies comparing lithium with placebo and other drugs. The current status of lithium prophylaxis in various disorders is examined and the need for further research discussed. 31 references. (Author abstract)

194746 Shelley, Edward M.; Medlewicz, Julien; Fieve, Ronald R. Columbia University College of Physicians & Surgeons, New York, NY **Affective disease health maintenance or-**

ganization: patterns of lithium response. New York State Journal of Medicine. 74(10):1766-1768, 1974.

The patterns of lithium response in an affective disorder health maintenance organization were studied. Twenty patients participated in a longitudinal study of the potential of lithium in preventing affective illness. Fourteen of the patients remained free of affective episodes during this period and never required the services of a psychiatrist. The six patients who required additional services of a psychiatrist had a significantly lower incidence of a family history of mania than the other 14 patients. The presence of manic episodes in the patient's family was related to a near absence of treatment problems. 3 references. (Author abstract modified)

194862 Weiss, Brian L.; Foster, F. Gordon; Reynolds, Charles F., III; Kupfer, David J. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15261 **Psychomotor activity in mania.** Archives of General Psychiatry. 31(3):379-383, 1974.

The levels of psychomotor activity during mania were investigated and the effects of lithium carbonate and clinical change on activity levels were assessed. Activity data were collected continuously by means of a telemetric mobility sensing system. The study was divided into three sections: the monitoring of three manic patients during a pretreatment baseline period; the study of six bipolar patients before and during lithium carbonate treatment; and the intensive longitudinal investigation of a manic patient over a 5 month period. Results indicate that both the quantity and patterning of manic activity were substantially different from other diagnostic groups previously studied. Activity levels do not appear to be affected by the use of lithium carbonate, unless associated with clinical change. 27 references. (Author abstract)

195040 Ossofsky, Helen J. 133 Merrie Ridge Road, McLean, VA 22101 **Amenorrhea in endogenous depression.** International Pharmacopsychiatry (Basel). 9(2):100-108, 1974.

Five patients are presented in whom reproductive abnormalities (amenorrhea) and depression were both reversed with imipramine. It is suggested that although much clinical and experimental work lies ahead before the relationship of hypothalamic hormones and depression is understood, current research pertaining to hypothalamic releasing factors provides many clues which fit quite well with both clinical observations and current theories regarding a neurodendocrinological pathogenesis of depression. 15 references. (Author abstract)

195041 Saarma, J.; Saarma, M.; Sild, L.; Tikk, P. Staadioni 48, Tartu, Est. SSR, USSR **Effect of thiothixene upon the higher nervous activity in chronic schizophrenics.** International Pharmacopsychiatry (Basel). 9(2):109-117, 1974.

The clinical effects of thiothixene and its action upon the higher nervous activity (HNA) were investigated in a sample of 22 chronic schizophrenic patients (mean duration of the disease 9.6years). In three patients there was a good, and in nine patients there was a moderate, clinical improvement. In HNA there was a marked improvement of the stability of excitatory process, of the equilibrium of excitatory and inhibitory processes and of internal inhibition. Some of the HNA parameters reflecting the intensity of transmarginal inhibition were found to be of prognostic value. 26 references. (Author abstract)

195533 Belsanti, Rodolfo; Calo, Antonio. Ospedale Psichiatrico Inteprovinciale Salentino -- Lecce, Italy **/Experience with monoclorimipramine (Anafranil) in psychiatry./** Esperienza con Monoclorimipramina (Anafranil) in psichiatria. Rivista di Psichiatria (Roma). 7(6):448-458, 1972.

The effectiveness of the drug chlorimipramine (Anafranil), administered intraveneously, in the treatment of patients showing depressive syndromes, neuroses, catatonic dissociative syndromes or mixed psychosis is described. Favorable results obtained by numerous doctors are listed. Twenty one cases involving uasge of the drug are discussed. 15 references. (Author abstract modified)

195617 Rao, K. Bhujanga. Kurnool Medical College, Kurnool, A.P., India **Trimipramine ('surmontil') -- clinical evaluation in depression.** Antiseptic (Madras). 69(12):867-870, 1972.

The dosage, potency and efficacy of Trimipramine in relieving depressive illness was assessed. The duration of treatment required to obtain clinical response was studied in 30 outpatients of both sexes over a 4 month period. A rapid lift in mood was reported, though neurotic depression showed only fair response. Anxiolytic and soporific properties are noted. Side-effects were negligible and it is concluded that surmontil has advantages over other available antidepressants. Patients who did not respond to other drugs did respond to Trimipramine. 11 references. (Journal abstract modified)

195916 Rifkin, Arthur; Quitkin, Frederic; Blumberg, Arnold G.; Klein, Donald F. Box 38, Glen Oaks, NY 11004 **The effect of lithium on thyroid functioning: a controlled study.** Journal of Psychiatric Research (Oxford). 10(2):115-120, 1974.

The effects of lithium on thyroid function were examined by treating patients with emotionally unstable character disorder for 6 weeks with lithium carbonate and for 6 weeks with placebo, with random assignment to sequence. Protein bound iodine (PBI), 11 patients; T-4 by resin column, 12 patients; and, the uptake after 24 hour of I131 (RAIU), 10 patients, were obtained during the sixth week of each drug period. Compared to the placebo period, during the lithium period, there was a statistically significant fall in PBI, and T-4, and increase in RAIU. Except for T-4, comparison of the lithium period to baseline values revealed the same findings. These findings are compatible with a direct depressing effect of lithium on the release of thyroid hormone. There was no relationship between the lithium effect on the thyroid and clinical response of the mood disorder associated with the psychiatric illness. 9 references. (Author abstract modified)

195918 Chernik, D. A.; Cochrane, C.; Mendels, J. Dept. of Psychiatry, Univ. of Pennsylvania, Philadelphia, PA **Effects of lithium carbonate on sleep.** Journal of Psychiatric Research (Oxford). 10(2):133-146, 1974.

The effect of lithium carbonate on the sleep of 17 psychiatric patients was studied for 496 nights. Lithium carbonate appeared to normalize the sleep of depressed patients, significantly increasing the low baseline levels of percent delta wave sleep and significantly decreasing the somewhat elevated levels of percent stage 1 REM sleep. There were significant positive and negative regression slopes for percent delta and REM sleep with increasing plasma lithium levels. The sleep changes frequently occurred within 24 hours after the initiation of lithium carbonate treatment and the withdrawal of lithium during the study was associated with an immediate change in both percent stage 1 REM and delta wave sleep in the direction of baseline values in spite of sustained clinical improvements, strongly suggesting that the changes in sleep were directly related to the presence of lithium rather than to clinical change. 49 references. (Author abstract modified)

195924 Bowers, Malcolm B., Jr. Department of Psychiatry, Yale University, New Haven, CT **Clinical measurement of central dopamine and serotonin metabolism in acute psychotic disorders.** Journal of Psychiatric Research (Oxford). 10(2):152, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,research to determine the status of central 5HT and DA metabolism before and during treatment with antipsychotic drugs in protracted drug induced and nondrug induced psychoses was described. Probenecid induced increases in lumbar CSF 5HIAA and HVA were used as indicators of central metabolism of the corresponding amines. The findings were that in a series of extended psychotic reactions, probably triggered by LSD use, evidence was found of decreased 5HIAA formation. In nondrug induced cases some tentative evidence was found for different metabolite patterns in the 'good premorbid' as compared to 'poor premorbid' cases. Clinical ratings of psychotic disorganization and usual thoughts were found to correlate best with pretreatment 5HIAA values. A nearly significant negative correlation between pretreatment HVA levels and phenothiazine dose during remission of the psychosis was also found. (Journal abstract modified)

195931 Mendels, J.; Frazer, A.; Cochrane, C.; Bianchi, P. University of Pennsylvania, Philadelphia, PA **Sodium and lithium erythrocyte concentration in affective disorders.** Journal of Psychiatric Research (Oxford). 10(2):157, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C. a study of sodium (Na) and lithium (Li) red blood cell (RBC) concentrations in depressed and manic patients carried out to examine the role of lithium in patients with affective illnesses was reported. The following observations were made: (1) the depressed patients who improved with Li treatment had significantly higher RBC Li concentrations and significantly higher RBC; (2) in general RBC Na increased with Li administration; and (3) there was a negative correlation between RBC Li and Na concentration and Beck Depression Inventory Scores. (Journal abstract modified)

195932 Heninger, George R. Department of Psychiatry, Yale University, New Haven, CT **Neuropsychologic mechanisms of lithium therapy.** Journal of Psychiatric Research (Oxford). 10(2):157-158, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,the neuropsychologic mechanisms of lithium therapy were discussed and a study which examined the observation that during lithium treatment there is a mild but significant decrement in visual psychomotor performance was described. It was found that lithium therapy was associated with a reduction in manic symptomatology, and increase in EEG theta intensity, and increase in somatosensory evoked response amplitudes with an alteration of their temporal recovery functions, and a consistent reduction of speed of performance on a finger dexterity test and speed of performance on a visual motor digit symbol substitution test. It was concluded that the data support the hypothesis that an important mechanism involved in the therapeutic effect of lithium on manic symptomatology is a unique type of cortical synchronization. (Journal abstract modified)

196042 Beckmann, Helmut; St.-Laurent, Jacques; Goodwin, Frederick K. Section on Psychiatry, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **The effect of lithium on urinary MHPG in unipolar and bipolar depressed patients. (Unpublished paper).** Bethesda, Md., NIMH, 1974. 19 p.

The effect of lithium on urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) was examined in unipolar and bipolar depressed patients. A 24 h urinary excretion of MHPG was studied longitudinally in 10 depressed patients before and during the acute and chronic phases of lithium treatment. Five of the Ss were identified as bipolar I (prior history of mania), three as bipolar II (history of hypomania) and two as unipolar (history of depression). During acute lithium administration there was no consistent pattern of change in MHPG. Comparing the predrug period with the third and fourth week of treatment, all of the responders showed an increase in MHPG while the nonresponders showed no change or a decrease. It is concluded that the change in clinical state is the most important variable contributing to MHPG changes in these patients. 35 references. (Author abstract modified)

196149 Mori, Atsuyoshi. Department of Neuropsychiatry, School of Medicine, Toho University, Omori, Tokyo, Japan **Recent therapeutic aspects of depression especially on the drug therapy.** Journal of the Medical Society of Toho University (Tokyo). 20(5/6):489-495, 1973.

The mechanism of action of the new antidepressants on brain amine metabolism is described, as well as a short history of this type of drug therapy. The international classification and various rating scales of depression are introduced, and the structure of the symptoms of depression is shown, following application of Zung's Self-rating Depression Scale to 59 depressive subjects. Three main therapeutic actions of antidepressants are identified and the classification of new drugs along this spectrum of action is described. The clinical use of antidepressants in 185 cases is summarized and compared with literature data. The possibilities of new antidepressants and the use of drug therapy in treatment of depression are discussed. 18 references. (Journal abstract modified)

196679 Ayd, Frank J., Jr. International Drug Therapy Newsletter, 912 West Lake Ave., Baltimore, MD 21210 **Once-a-day dosage tricyclic antidepressant drug therapy: a survey.** Diseases of the Nervous System. 35(10):475-480, 1974.

The once a day administration of tricyclic antidepressants by psychiatrists was surveyed in a questionnaire mailed to 1000 psychiatrists in 50 states. A telephone followup was made of 75 randomly chosen individuals in private practice and among hospital psychiatrists. Results disclosed a high percentage of prescribers of single daily dosages for a large patient population, many of whom had been treated for 3 months to 1 year or longer, often with dosages in excess of those in the package insert for each drug. There were no significant differences of opinion among respondents with respect to tolerance, safety, efficacy, advantages, disadvantages and economy of this method of treatment. All respondents acknowledged that there was a minority of depressed patients for whom this therapy was unsuitable. For maintenance therapy, 81% consider single daily dosage treatment of depression efficacious; for initial therapy, 51%. 12 references. (Author abstract modified)

196680 Kline, N. S.; Shah, B. K. no address **A pattern of antidepressive effect of tryptophan & imipramine in males & females.** Diseases of the Nervous System. 35(10):481-483, 1974.

A methodological procedure for combining mathematical and clinical statistics to explicate biological differences in therapeutic changes due to tryptophan and imipramine is re-

ported. Thirty four patients, in the active depressive phase, were randomly chosen for the study and assigned either to tryptophan treatment or to imipramine. Results show that there was no interaction between sex and drug; in average therapeutic rating tryptophan was as effective as imipramine; and for a given dosage average therapeutic ratings in female patients were significantly lower than that of male patients for both drugs. 2 references. (Author abstract modified)

197031 Lauritsen, Bent J.; Madsen, Hanne. Psychochemistry Institute, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark **A multinational, double-blind trial with a new antidepressant maprotiline (Ludiomil) and amitriptyline.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(2):192-201, 1974.

A multinational double-blind trial in which the tetracyclic antidepressant maprotiline (Ludiomil) was compared with amitriptyline is reported. Two hundred and eleven patients participated and were diagnosed as cases of endogeneous depression, and reactive or other depressions. No statistically significant differences in antidepressive effect was assessed by Total Hamilton Score, and global evaluation was found between maprotiline and amitriptyline. A significant difference in favor of maprotiline was shown in the global evaluation of unwanted effects and in regard to individual symptoms such as blurred vision and sweating. Laboratory tests showed no positive difference between the two preparations. Multicenter trials are discussed and further research is suggested. 10 references. (Author abstract modified)

197033 Roelofs, Gerard A. Centre for the Mentally Handicapped, Hernesseroord, Middelharnis, The Netherlands **Penfluridol (R 16 341) as a maintenance therapy in chronic psychotic patients: a double-blind clinical evaluation.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(2):219-224, 1974.

A double-blind, 6 month trial of penfluridol and placebo was conducted in 15 chronic psychotic patients aged 25 to 64 years. The patients, who had been well controlled with penfluridol for several months, were subdivided into two comparable groups with seven Ss receiving penfluridol and eight receiving placebo. Dexetimide and other nonpsychotropic drugs already taken before the trial were continued. Assessment was made after 1, 2, 4 and 6 months. At the end of the trial, results show that the penfluridol treated Ss maintained their improvement and placebo treated Ss had deteriorated regarding direct psychotic phenomena and general behavior. 9 references. (Author abstract modified)

197035 Lingjaerde, Odd; Edlund, A. H.; Gormsen, C. A.; Gottfries, C. G.; Haugstad, A.; Hermann, I. L.; Hollnagel, P.; Makimattila, A. Asgard Hospital, 9010 Asgard, Norway **The effect of lithium carbonate in combination with tricyclic antidepressants in endogenous depression: a double-blind, multicenter trial.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(2):233-242, 1974.

Forty five endogenously depressed patients in nine different hospitals were randomly given tricyclic antidepressants plus placebo or tricyclic antidepressants plus lithium carbonate, for a maximum of 4 weeks. At one hospital, the six Ss in the lithium group showed significantly greater improvement after 1 and 4 weeks than the seven Ss in the placebo group. No differences were seen in the other hospitals. Treatment response in the total material did not correlate significantly with diagnosis, age or sex. No significant side-effects were reported. Lithium did not antagonize but seemed to enhance the therapeutic effect of tricyclic antidepressants. Recommendations for its use are included. 25 references. (Author abstract modified)

197209 Fujiwara, Jiro; Otsuki, Saburo. Dept. of Neuro-Psychiatry, Okayama Univ. Medical School, Okayama, Japan **Subtype of affective psychoses classified by response on amine precursors and monoamine metabolism.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(2):93-100, 1974.

A subtype of affective psychoses is classified by response to amine precursors and monoamine metabolism. Twenty cases of depression were treated with L-5-hydroxytryptophan (L-5HTP) and 17 cases were treated with L-dihydroxyphenalanine (L-DOPA); the treatment was effective in 50% and 29% of Ss respectively. The depression which responded to L-5HTP was classified as IA type (indoleamine type) while the CA type (catecholamine type) responded to L-DOPA. Before treatment, the IA type showed marked agitation or anxiety and insomnia while the CA type showed severe psychomotor retardation such as muteness, absence of motor activity and a tendency to hypersomnia. The content of 5-hydroxyindoleacetic acid in the cerebrospinal fluid was lower in IA type than in controls. 36 references. (Author abstract modified)

197531 Prien, Robert F.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Laboratory, Veterans Administration Hospital, Perry Point, MD **Lithium prophylaxis: a critical review.** Comprehensive Psychiatry. 15(5):357-363, 1974.

The efficacy of lithium prophylaxis in recurrent affective illness in comparison with placebo and control medication is discussed. All of the eight research studies described in which lithium - placebo therapeutic comparisons were made concluded that lithium had a significantly greater affect in preventing relapse into affective illness, whether patients were manic-depressive (bipolar) or suffered from depression without mania (unipolar). In the two research studies described in which lithium was compared with control medication (imipramine), results were mixed. In one study, results were inconclusive due to methodological problems. In the other study, bipolar patients responded better to lithium, while unipolar patients responded equally well to lithium and to imipramine. Three important factors in appraising the prophylactic efficacy of lithium are as follows: (1) a definition of prophylactic effectiveness; (2) frequency of lithium therapy necessary for psychiatric patients who have only occasional attacks; and (3) the necessity for comparison of lithium with other control medications and on a more long-range basis. 31 references.

197532 Gershon, Samuel. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, New York, NY **Lithium prophylaxis in recurrent affective disorders.** Comprehensive Psychiatry. 15(5):365-373, 1974.

The efficacy of lithium prophylaxis in recurrent affective disorders is discussed and the literature on the subject is reviewed. Of the seven controlled studies comparing lithium carbonate with placebo treatment, all but one conclude that lithium is more effective than placebo. Of the two trials comparing lithium with imipramine, one study found that neither drug exerted a major prophylactic effect; the other study, which compared lithium, imipramine, and placebo therapy, found clear superiority of the two drugs over placebo. It is concluded that lithium treatment does have a positive effect in recurrent affective disorders but the definition of prophylaxis in the case of lithium, the effect of modified lithium dosage,

the paucity of data on comparisons of lithium with other drugs, and the degree of efficacy of lithium maintenance medication for schizoaffectives are still unresolved. 35 references.

197600 Sternlicht, Manny; Rosenfeld, Pincus; Siegel, Louis. Willowbrook State School, Staten Island, NY 10314 **Retesting with graphic production: resolution of a diagnostic dilemma.** Art Psychotherapy. 1(3/4):299-300, 1973.

A case study demonstrates how the employment of a drug may disguise or distort certain personality characteristics and how an accurate diagnosis is secured and confirmed by means of graphic reproduction after discontinuance of the drug. Upon institutionalization, the subject was placed on Permitil and evaluated both psychologically and psychiatrically. The psychologist's diagnostic impression was of psychoneurosis and reactive depression. The psychiatrist's diagnosis was schizophrenia, paranoid type. Three months later the drug was discontinued and a psychological reevaluation 2 weeks after the discontinuance confirmed the psychologist's diagnosis of psychoneurosis and provided comparative evidence of the patient's overall improvement, as illustrated by his before and after drawings of a house and a man standing in the rain.

197856 Schulterbrandt, Joy G.; Raskin, Allen; Reatig, Natalie. Center for Studies of Child and Family Mental Health, NIMH, Parklawn Building, Rm. 12C-24, 5600 Fischers Lane, Rockville, MD 20852 **True and apparent side effects in a controlled trial of chlorpromazine and imipramine in depression.** Psychopharmacologia (Berlin). 38(4):303-317, 1974.

Five hundred and fifty five acutely depressed patients receiving chlorpromazine and imipramine, were studied to determine the incidence and severity of drug related side-effects. The ability of clinicians to distinguish between drug related side effects and symptoms considered natural to the depressive illnesses was also investigated. The results indicate that side-effects were minimal for both active drug groups and that among the dropouts for serious side-effects (31 cases) the majority were receiving chlorpromazine. Skin rash and hypotension were the most frequent reasons cited for side-effect terminations from the study. It appeared that clinicians were generally able to distinguish drug related side-effects from symptoms usually associated with depression. There was some indication, however, that they tended to rate as non-medication related, certain symptoms which were actually drug induced. The latter included muscle rigidity, edema, and dry mouth on chlorpromazine and tremulousness on imipramine. 17 references. (Author abstract)

198029 Burrows, Graham; Scoggins, Bruce A.; Turecek, L. R.; Davies, Brian. Department of Psychiatry, University of Melbourne, Melbourne, Australia **Plasma nortriptyline and clinical response.** Clinical Pharmacology and Therapeutics. 16(4):639-644, 1974.

The relationship of plasma nortriptyline levels to the clinical response of 80 depressed patients was studied. Plasma nortriptyline levels were estimated 4 weeks after commencing treatment. Percentage change in the Hamilton Depression Rating Scale was used to measure clinical response. There was no simple relationship between these two measures. Twelve of the 80 patients were studied further. Clinical response to variations of plasma nortriptyline levels was studied. Calculation of regression coefficients showed a positive relationship between clinical change and plasma nortriptyline levels in all. Comparison of the regression coefficients showed that they differed significantly among themselves and were not related to age or sex. 16 references. (Author abstract)

10 DRUG TRIALS IN NEUROSES

193412 Krivda, Joseph F. Medical Associates of New Paltz, New Paltz, NY **Major or minor tranquilizers for relief of common symptoms of psychoneurosis?** Journal of Psychiatric Nursing and Mental Health Services. 12(4):28-33, 1974.

Thioridazine is shown to alleviate anxiety and depression, and other bothersome symptoms associated with neurotic anxious and depressive reactions, better than diazepam. This refutes the opinion sometimes voiced that minor tranquilizers are more effective than major tranquilizers for these symptoms. The response in the thioridazine patients was significantly better for overall change, for the Hamilton scale psychic factor and for the anxiety, depression, tension, cognitive impairment, and interview behavior items of the Hamilton scale. Data from the patients' ratings confirmed these physician evaluations. No matter which analytic method was used, for only one item on any of the scales was there a significantly better response in the diazepam patients. None of the patients in either group reported side-effects. 11 references. (Author abstract modified)

194045 Rickels, Karl; Weise, Charles C.; Clark, E. L.; Jenkins, B. Wheeler; Rose, Charles K.; Rosenfeld, Howard; Gordon, Paul E. University of Pennsylvania, Philadelphia, PA **Thiothixene and thioridazine in anxiety.** British Journal of Psychiatry (London). 125:79-87, 1974.

A total of 155 anxious neurotic outpatients participated in a double-blind drug trial of thiothixene, thioridazine, and placebo. Findings indicate that thioridazine produces the most and placebo the least amount of side-effects. A few significant trends for both active drugs to produce more improvement than placebo appeared after 2 weeks but not after 4 to 6 weeks of treatment. Findings suggest that while initial level of anxious and overall neurotic psychopathology has no differential effect on treatment outcome, initial level of secondary depression has a mild effect, both drugs producing more improvement in the initially high than in the initially low depressed anxious patient. It is concluded that the usefulness of thiothixene and thioridazine as antianxiety agents must be considered at best rather limited. 17 references. (Author abstract modified)

194276 Kishore, Baldev; Kaur, A.; Verma, R. S. Punjab Mental Hospital, Amritsar, India **A comparative study of doxepin versus trifluoperazine in anxiety neurosis.** Journal of the Indian Medical Association (Calcutta) 60(8):280-284, 1973.

A double-blind crossover trial with doxepin hydrochloride and trifluoperazine in 20 anxiety neurosis patients is reported. Doxepin hydrochloride is an effective anxiolytic drug; compared to trifluoperazine, its anxiolytic effect is lower but its antidepressive properties are higher. Doxepine hydrochloride is more effective than trifluoperazine in the control of suicidal ideas, sleeplessness, and in uplifting retardation, and it is a much safer and better tolerated drug than trifluoperazine. 7 references.

194556 Khurana, Anand Bhushan; Sharma, Shridhar. Goa Medical College, Baroda, India **Treatment of anxious patients with nealbarbitone -- ('Censedal').** Antiseptic (Madras). 68(5):349-353, 1971.

Patients with anxiety states were controlled through the use of nealbarbitone. The drug was used in a 180 to 360mg daily dosage to treat 20 outpatients under uncontrolled conditions. Eleven patients showed mild to optimal improvement, though

eight of them showed only a slight improvement. Clinical evidence has shown that the drug is effective when anxiety is not too profound and that its temporary use may be helpful in any comprehensive psychotherapeutic treatment program. 4 references. (Author abstract modified)

194558 Kishore, Baldev; Kaur, A.; Verma, R. S. Punjab Mental Hospital, Amritsar, India **Comparative study of diazepam vs. chlordiazepoxide in anxiety neurosis.** Antiseptic (Madras). 69(2):101-108, 1972.

Twenty patients with anxiety neurosis and depression as an associated symptom were studied in a cross-over trial with diazepam (Calmpose) and chlordiazepoxide. Calmpose was effective in 45% of the patients studied, but chlordiazepoxide relieved anxiety symptoms in only 15%. In the associated depressive symptoms, 43.7% improved on Calmpose and only 18.7% on chlordiazepoxide. The patients selected for trial were the difficult to treat cases. No psychotherapy was given to these cases while on drug trial. 7 references.

194719 Masters, Roshen S.; Kajaria, S. M.; Raheja, Sheila. B. J. Medical College and Sassoon General Hospital, Poona, India **A controlled evaluation of 'lorazepam' and diazepam in anxiety neurosis.** Indian Journal of Psychiatry (Madurai). 16(1):42-47, 1974.

The efficacy of lorazepam and diazepam in anxiety neurosis was compared in a double-blind study of 60 outpatients. Assessment of anxiety was done on Hamilton's scale over a formal trial period of 4 weeks. At the end of 2 weeks, lorazepam reduced the mean score on Hamilton's Scale by 60% and diazepam by 44%. Of the patients tested, 69% on lorazepam and 40% on diazepam had a satisfactory response at this time. By the end of the 4 weeks, the mean score reductions were 70% and 64% on lorazepam and diazepam, respectively, and a satisfactory response occurred in 81% and 75% of patients, respectively. The incidence of drowsiness was low with both drugs and none of the patients had hemopoietic, renal or hepatic toxicity. Lorazepam and diazepam were effective anxiolytics but a clinically satisfactory response was found earlier with lorazepam. 5 references. (Author abstract modified)

194834 Goldberg, Harold L.; Finnerty, Richard J.; Nathan, Leon; Cole, Jonathan O. West-Ros-Park Mental Health Center, Boston State Hospital, Boston, MA 02124 **Doxepin in a single bedtime dose in psychoneurotic outpatients.** Archives of Genral Psychiatry. 31(4):513-517, 1974.

The efficacy of doxepin when given only at bedtime for the treatment of patients with mixed anxiety/depression was assessed in a 4 week double-blind study with 41 psychoneurotic outpatients. Scales used were the Lipman-Rickels Scale, the Psychiatric Outpatient Mood Scale, the Hamilton Anxiety Scale, and the Finnerty-Goldberg Sleep Evaluation Scale. The results of this study indicated that doxepin, given at bedtime, is significantly more effective than a placebo in treating mixed anxiety/depression, as shown by all three psychiatric rating scales used and by overall evaluation, even when the improvement is controlled for pretreatment correlates of improvement. The prediction model indicated that subjects with higher occupational levels, more severe Hamilton mental rating, and less severe Hamilton behavior rating, were more likely to improve. Bedtime dosing seemed to accelerate the antidepressive effect of doxepin while yielding significant improvement in sleep patterns. 9 references. (Author abstract modified)

195532 Lalli, Nicola. Istituto di Psichiatra, Universita di Roma, Rome, Italy /**Experimentation with Sulpiride in cases of psychoneurosis.**/ Sperimentazione della Sulpiride nelle psiconevrosi. Rivista di Psichiatria (Roma). 7(6):434-447, 1972.

The drug sulpiride was tested in various cases of neurosis and precise and differentiated features are discussed. In cases of depression and anxiety sulpiride appears to act quickly. In cases of free anxiety and obsessive syndromes the action of sulpiride is minor. 46 references. (Author abstract modified)

195616 Narang, R. L. Department of Psychiatry, Dayanand Medical College, Ludhiana, India **Surmontil -- in depression** Antiseptic (Madras). 70(11):685-688, 1973.

The therapeutic effects, time intervals, and side-effects of the tricyclic antidepressant, trimipramine, were studied. Thirty patients suffering from depression and insomnia were treated with trimipramine for up to 1 year. Most of the patients did respond to treatment, with a recovery rate over 80% in depressed patients. Insomnia decreased in 50% of the patients. No serious side-effects were noted. The lift in depression came between 3 days and 3 weeks after initiation. 4 references.

195618 Menon, M. Sarada; Badsha, Haneef Government Mental Hospital, Madras, India **Controlled clinical trial with diazepam.** Antiseptic (Madras). 70(3):171-178, 1973.

The effects of diazepam on anxiety neuroses in outpatients with depressive features were studied. Specific reference is made to somatic symptoms, psychological components and accompanying depression. Twenty controls were placed on oxazepam for the 6 week period under double-blind conditions. Diazepam proved to be an effective antidepressant and anxiolytic agent. Results indicate that diazepam is significantly superior in quick control of distressing anxiety, tension, and depression symptoms. It is a useful drug in gaining the confidence of the patient and rendering him more suitable for social readjustment, with a concommitant reduction in the duration of psychotherapy. The lack of side-effects is also predictive of the drug's utility. 5 references. (Journal abstract modifed)

195620 Suvarna, G. C. K. R. Hospital, Mysore, India **Surmontil (trimipramine) -- a clinical trial.** Antiseptic (Madras). 69(9):637-644, 1972.

The efficacy of Surmontil in the treatment of depression during a 6 month study was assessed. Sixty eight depressive outpatients in India were evaluated by investigators for improvement of symptoms. Almost 50% of the patients showed excellent recovery. The most effective dosage of Surmontil varied with the severity of the depression and the person, with side-effects minimal in most Ss. Educated patients adhered more closely to the dosage and improvement was greater. Reference is made to earlier clinical trials with other antidepressants. 16 references. (Journal abstract modified)

195621 Rao, A. Venkoba; Sridhar, Chandraprasad; Chinnian, Rawalin. Department of Psychiatry, Madurai Medical College, India **Lorazepam in anxiety neurosis.** Antiseptic (Madras). 70(2):103-107, 1973.

Lorazepam was investigated in order to assess its usefulness in anxiety neurosis. An open trial was used with 20 patients. Psychological assessment was carried out using Hamilton's scale and global improvement scores are reported. It was found that anxious moods, tensions, insomnia, and somatic complaints were significantly relieved. It is concluded that Lorazepam is an effective, well tolerated anxiolytic when used in a dose of 2 to 6 mg per day. Some anatomical, cardiovascu-

lar and other behavior complaints were also favorably influenced. 7 references.

195929 Prange, A. J.; Wilson, L. C. Research Development Section, University of North Carolina School of Medicine, Chapel Hill, NC **Thyrotropin releasing hormone (TRH) in depression: a preliminary report.** Journal of Psychiatric Research (Oxford). 10(2):155-156, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,a study of eight depressed women whose results suggest that a single i.v. injection of thyroptropin releasing hormone (TRH) produces prompt, brief relief from depression was reported. It was concluded that TRH has a direct central effect and that evidence points away from its antidepressant effect being thyroid mediated. (Journal abstract modified)

196191 Dasberg, Haim. Gaza Road 35, Jerusalem, Israel **The effect of daily oral dosage of diazepam, plasma concentrations and metabolic clearance of diazepam and demethyldiazepam on various constituents of the acute clinical anxiety syndrome.** Psychotherapy and Psychosomatics (Basel). 24(2-3):113-118, 1974.

In a study of the effects of diazepam and demethyldiazepam on clinical anxiety syndrome, 20mg of diazepam daily, for 5 days, was given as a short-term adjunctive treatment to crisis patients, and was not different from placebo, except for patients with high levels of anxiety. However, some specific symptoms are diazepam sensitive, such as insomnia, respiratory, gastrointestinal complaints, and the cluster of the 'three main symptoms'. The minimal effective plasma concentration for these symptoms is 400ng/ml of diazepam. N-demethyldiazepam levels of 300ng/ml and above are disturbing. The main conclusion is that monitoring the dosage by checking plasma levels, as elsewhere in psychopharmacology seems advisable also for diazepam treatments of anxiety. 9 references. (Author abstract modified)

198040 Wheatley, David. General Practitioner Research Group, Twickenham, England **Psychiatric aspects of hypertension.** Psychopharmacology Bulletin. 10(2):4-5, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which examined the possibility of an association between psychiatric morbidity and hypertension. Both new and old cases of hypertension had more anxiety symptoms than the respective controls. In the old hypertensive cases, there were significantly more medical conditions directly associated with the hypertension than in the respective controls. Lowering the blood pressure did not relieve anxiety symptoms. Concomitant treatment with an antianxiety drug as well as antihypertensive medications is suggested for better relief of anxiety symptoms, better control of systolic blood pressure, and a reduction in the complications associated with the hypertension. (Journal abstract modified)

198046 Silverstone, J. Trevor. St. Bartholomew's Hospital, London, England **Some new approaches to the treatment of anxiety.** Psychopharmacology Bulletin. 10(2):10-11, 1974.

At the Early Clinical Drug Evaluation Unit's meeting in May 1973, a paper was presented which reported on the relative anxiolytic properties of a beta-adrenergic blocker (oxprenalol) and a centrally acting compound (Benzoctamine). Patients received either oxprenalol (Trasicor) and placebo, benzoctamine (Tacitin) and placebo, both drugs of two placebos. Anxiety was measured by self-ratings, the Morbid Anxiety Inventory, and a global observer rating. All four groups improved; but the benzoctamine group showed the greatest improvement and also the greatest side-effects. It was concluded that centrally acting anxiolytics are more effecting in relieving anxiety than beta-blockers. 3 references. (Journal abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

192988 Block, C.; Borendal-Jansson, B.; Carlsson, C. Lillhagen Mental Hospital, 42203 Hisings Backa 3, Sweden A **double-blind crossover comparison between clothiapine and diazepam in the treatment of mental symptoms in chronic alcoholics.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(4):321-325, 1974.

The effects of clothiapine and diazepam on anxiety, tension, irritability and depression in 35 chronic alcoholics were compared in a double-blind crossover study. The duration of treatment was 1 week with each product in randomized order. Patients were examined prior to the study, after 1 week and after 2 weeks. Of 30 patients beginning the trial, 12 were on medium dose, 10 on low dose, and eight dropped out. Results of global scores by questionnaire showed that the majority of patients improved with both products. No significant differences between clothiapine and diazepam were observed, but tiredness and euphoria were reported in medium doses. Results suggest that neuroleptics in low doses may be equally effective as benzodiazepines in the treatment of chronic alcoholics. 6 references. (Author abstract modified)

193093 Raskin, Allen. Psychopharmacology Research Branch, NIMH, Parklawn Bldg., 5600 Fishers Lane, Room 9-101, Rockville, MD 20852 **Age-sex differences in response to antidepressant drugs.** Journal of Nervous and Mental Disease. 159(2):120-130, 1974.

Age - sex differences were examined in two multihospital collaborative studies of drug treatment in depression. The patients were divided into above and under 40 years age groups and were receiving treatment with either chlorpromazine, imipramine, diazepam, phenelzine, or a placebo. Results after 3 weeks of treatment showed: 1) older males responded better to active rather than placebo treatment; 2) older females were more selective and did well only on imipramine; 3) imipramine was not useful in younger women, who responded well on placebo; and 4) young males had a mixed response to placebo with placebo worse in patient groups where chlorpromazine was the active therapy. These results indicate that an analysis of sex differences alone could prove misleading, since there were as many differences in drug response between younger and older women and between younger and older men as there were between the sexes. 41 references. (Author abstract modified)

193291 Prien, Robert F.; Haber, Paul A.; Caffey, Eugene M., Jr. Central Neuropsychiatric Research Lab., Veterans Administration Hospital, Perry Point, MD **Psychoactive drug use in elderly patients with psychiatric disorders: a survey of 12 Veterans Administration Hospitals.** Perry Point, MD, Veterans Admin. Hospital, 1974. 17 p.

A survey conducted at 12 Veterans Administration Hospitals found that 778 (61%) of the 1276 elderly psychiatric patients were being treated with psychoactive drugs. Drug prescription practices relating to choice of drugs, prevalence of drug use, dosage, polypharmacy, and antiparkinson drug therapy are examined in terms of patient characteristics such as age and

diagnosis. These practices are also discussed in terms of the psychoactive drug literature, particularly as it pertains to elderly populations. 19 references. (Author abstract modified)

194043 Smulevitch, A. B.; Zavidovskaya, G. I.; Igonin, A. L.; Mikhailova, N. M. Institute of Psychiatry, U.S.S. R. Academy of Medical Sciences, Zagorodnoye Shosse 2, Moscow M-152, U.S.S.R. **The effectiveness of lithium in affective and schizo-affective psychoses.** British Journal of Psychiatry (London).). 125:65-72, 1974.

The effectiveness of lithium in affective and schizoaffective disorders was studied. Methods of lithium preventative therapy used at the Institute of Psychiatry in Moscow are detailed. The dangers of habituation and decrease in effectiveness in long-term medication are considered and comprehensive pharmacological studies on compounds of other sodium group metals are urged to combat this problem. 30 references.

194208 Stoychev, E. G. Military Hospital Stanke Dimitrov, Sofia, Bulgaria **/Results of treating children with nocturnal enuresis with imipramine (psychoforin)./** V''rkhy rezultatite ot lecheniyeto s psikhoforin na detsa, stradashchi ot noshchno nezad''rzhane na urinata. Nevrologiya, Psikhiatriya i Nevrokhirurgiya (Sofia). 12(6):423-427, 1973.

Results of treating nocturnal enuresis in children with imipramine (psychoforin) are reported. One quarter of the cases treated recovered fully; another quarter showed significant improvement; and a third quarter showed slight improvement. 23 references. (Author abstract modified)

194244 Bergmann, K. Brighton Clinic, Newcastle General Hospital, Newcastle upon Tyne 4, England **Assessment of therapy in psychogeriatric illness.** Gerontologia Clinica (Basel). 16(1-3):54-63, 1974.

Therapy in psychogeriatric illness is assessed and it is noted that such therapy must acknowledge the multifactioral nature of the illness, and that a pharmacological approach must be teamed with treatment of social, emotional and physical factors. Recommended treatment of disturbances due to organic psychosyndromes includes insightful management and correct dosages of sedatives such as phenothiazines. It is advocated that affective disorders a treated with environmental support, social manipulation and treatment of physical ill health with minimal doses of antidepressant drugs. Antidepressant drugs and tranquilizers and their use in psychogeriatric illness are reviewed. 11 references.

194311 D'Netto, T. B. Central and Eastern Commands, Indian Armed Forces, India **A clinical trial with thioproperazine (Majeptil M & B) -- a comparison with chlorpromazine.** Armed Forces Medical Journal (New Delhi). 28(1):69-75, 1972.

A clinical trial comparing the effectiveness of thioproperazine (Majeptil M & B) with chlorpromazine on violent/excited patients is reported. In 12 out of 20 cases (60%) on Majeptil, good improvement was achieved within 48 hours, as compared to 40% attaining the same standard of improvement on chlorpromazine. Of the cases on Majeptil tablets alone, 55.6% showed good improvement as compared to 26.7% of the cases of chlorpromazine tablets. Whereas 50% of the cases on Majeptil 5mg tds improved, only 10% of the cases on chlorpromazine 50mg tds improved. Sixty seven percent of the cases on Majaptil 10mg showed good improvement compared to 60% of the cases on chlorpromazine 100mg. Majeptil is therefore about 10 times more powerful than chlorpromazine. The most striking advantage of Majeptil was the rapidity with which it could bring the excited, violent patient under control with doses as low as 5-10mg orally three times daily. 5 references.

194475 Fuse, Seiichi; Yamada, Ryoji. Fuse Hospital, Japan **Administration of PG-501 for the treatment of extrapyramidal syndrome caused by the administration of a psychotropic drug.** Medical Consultation and New Remedies (Tokyo). 10(12):143-146, 1973.

The effect of PG-501 on tremor induced by psychopharmacological therapy was studied, based on an experiment with 27 schizophrenics, and five other patients with psychotic or neuromuscular disorders. Some decrease in tremor was noted in almost all subjects and, although some side-effects were observed, they were not conclusively traced to the drug therapy.

194509 Higuchi, Masamoto; Suminishi, Yu; Matsuzaki, Shuji; Nakatani, Hisashi; Ogihara, Masao; Kaneko, Hideo; Takahashi, Yoshihiko; Endo, Shigemichi. Tokyo Jikei-kai Medical School, Japan **Examination of the new psychotropic drug, Dogmatyl (FK-880-sulpiride).** Medical Consultation and New Remedies (Tokyo). 10(12):169-181, 1973.

The effectiveness of Dogmatyl (FK-880-sulpiride) in psychosomatic diseases was studied. Twenty seven patients with various psychosomatic diseases were treated with this drug, 150-300mg/day, for 7 to 77 days. Slight improvement was noted in anxiety, invitation, excessive tension and sleep disturbance. Another group of 27 patients with psychosomatic digestive disorders were treated with Dogmatyl, 300mg/day, for 4 to 60 days. Complaints of digestive disturbance lessened during use of the drug. Effects of treatment were noted within 3 to 21 days with the first group, and within 4 to 29 days with the second group. The larger dosage was found to be more effective. Minor drowziness was observed as a side-effect.

194510 Higuchi, Masamoto. Tokyo Jikei-kai Medical College, Japan **My experience with the use of a tranquilizer, Noritren, in the department of internal medicine psychosomatics.** Medical Consultation and New Remedies (Tokyo). 10(11):161-172, 1973.

The effect of the tranquilizer, Noritren, on psychosomatic diseases was studied, based on an experiment in which 24 patients with various psychosomatic diseases were orally treated with this drug, 30 mg/day, for 14 to 105 days. The drug was used with or without other tranquilizers. Three patients dropped out, and out of the remaining 21, the drug was extremely effective in 4.8%, effective in 57.1%, slightly effective in 23.8%, and noneffective in 14.3%. No significant difference in effect was observed between this drug alone and this drug combined with serenal. Noritren was effective in general fatigue, depression, lack of volition, and anxiety. A minor case of drowsiness was observed in one patient.

194554 Ghafoor, P. K. Abdul; Mammi, Imbichi; Naik, V. P. Medical College Hospital, Calcutta-8, India **Pyrithioxine (encephabol) in mentally deficient children (a trial on 50 cases).** Antiseptic (Madras). 68(2):93-96, 1971.

Fifty mentally defective children between the ages of 1 and 15 years were treated with pyrithioxine. Promising results were obtained in 56% of the patients treated. Patients with mongolism, microcephaly, and diplegia did not respond to this drug. The only toxic effect noticed was motor restlessness in four children; two of these were controlled with a tranquilizer. 8 references. (Author abstract modified)

194710 Varma, Satish C.; Kemph, John P. State University of New York, Downstate Medical Center, New York, NY **The use of haloperidol in the treatment of a psychotic child with multiple tics: a case report.** Indian Journal of Medical Sciences (Bombay). 25(4):257-259, 1971.

Treatment of hyperactivity of an 11-year-old boy with haloperidol is reported. Previous medications had produced little effect on his symptoms and he had attended a school for emotionally disturbed children for 2 years with little positive effect. Prior to the use of this drug, tics were present almost constantly, but within 10 days after haloperidol was started, tics occurred less than 5% of the time. He became much more amenable to psychotherapy, producing more relevant material in interviews, and he was more cooperative with ward staff and other patients. Within 14 days after haloperidol was started, there was a total remission of tics and a rapid socialization of his behavior. 10 references. (Author abstract modified)

194758 Kline, N. S.; Wren, J. C.; Cooper, T. B.; Varga, E.; Canal, O. Research Center, Rockland State Hosptial, Orangeburg, NY 10962 **Evaluation of lithium therapy in chronic and periodic alcoholism.** American Journal of the Medical Sciences. 268(1):15-22, 1974.

The use of lithium as a therapeutic agent in the treatment of chronic alcoholic patients with depression was investigated in a double-blind study with active medication and placebo. Lithium appears to modify the patients' drinking habits significantly when the readmission rates of the groups are compared. Of those patients who had to be readmitted for their drinking, the lithium group had fewer episodes as compared to the control group. Although both groups were less depressed at the end of 1 year, there was not a significant difference between groups (analysis of covariance), ie, there was a placebo response which may have disguised a real difference. Other parameters studied include serum magnesium levels and thyroid function which showed that the clearance of iodine from the plasma by the thyroid gland was significantly increased. 9 references. (Author abstract)

195037 Appelt, M.; Floru, L. Rheinisches Landeskrankenhaus, Psychiatrische Universitatsklinik, Bergische Landstrasse 2, D-4012 Dusseldorf, Germany **/Experience with cyproteron acetate influence on human sexuality./** Erfahrungen uber die Beeinflussung der Sexualitat durch Cyproteronacetat. International Pharmacopsychiatry (Basel). 9(2):61-76, 1974.

The effects of cyproterone acetate administrated over a period of 6-18 months to 18 patients suffering from oligophrenia, schizophrenia or abnormal personality development were examined. Most of the patients were hospitalized through commitment. Cyproterone acetate proved to be an efficient clinical, home or ambulatory treatment, provided that the patient collaborated with it. Fear of punishment was the main cause why sexual abnormal oligophrenes took cyproterone acetate, as a social conscience could not be expected from this group of patients. Neurotic patients showed also a good response to the treatment. 20 references. (Author abstract modified)

195038 Haase, H. J.; Floru, L; Ulrich, F. Rheinisches Landeskrankenhaus, Psychiatrische Universitatsklinik, Bergische Landstrasse 2, D-4012 Dusseldorf, Germany **/A clinical-neuroleptic investigation of N-(1-ethyl-pyrrolidin-2-yl)- 2-methoxy-5-sulfamoyl-benzamid-neuroleptic Sulpiride (Dogmatil) in acutely ill schizophrenics./** Klinisch-neuroleptische Untersuchung des N-((1-Athyl-pyrrolidin-2-yl)- -methyl)-2-methoxy-5-sulfamoyl-Benzamid-neuroleptikums Sulpirid (Dogmatil) an akut erkrankten Schizophrenen. International Pharmacopsychiatry (Basel). 9(2):77-94, 1974.

Twenty six acute, first time or repeatedly diseased schizophrenic patients were treated by Sulpiride in a psychiatric ward. The method used was a variant of the single-blind technique of administration and evaluation. The substance proved to be an intermediary drug between feeble and middle potent neuroleptics. In doses about 200mg/day, it showed a mood clearing and stimulating effect. The average dosis necessary to reach the neuroleptic threshold was 399mg Sulpiride, the average time being 6 days. An average dosis of 593.3mg daily produced in an average time of 11.5days, dependent from the initial dose, an evident antipsychotic effect. A good indication for Sulpiride therapy seemed to be the inhibited and withdrawn patients, but also the restless, highly productive psychoses, of which 17 from 23 cases showed good results. Extrapyramidal side-effects were not important and could easily be kept under control. Only a certain drowsiness after very high doses was registered. The indication of Sulpiride in the ambulatory treatment and in postpsychotic depressions are discussed. 25 references. (Author abstract)

195155 Schneider, E.; Maxion, H.; Ziegler, B.; Jacobi, P. Abteilung fur Neurologie der Universitat, D-6000 Frankfurt a. M., Schleusenweg 2-16, Bundesrepublik, Germany **/Sleep in patients with Parkinson's disease and its influence by L-DOPA./** Das Schlafverhalten von Parkinsonkranken und seine Beeinflussung durch L-DOPA. Journal of Neurology (Berlin). 207(2):95-108, 1974.

Sleep in patients with Parkinson's disease and its influence by L-DOPA were examined. In 26 patients polygraphic night sleep recordings, prior to and following long-term administration of L-DOPA, were performed. There was a correlation between sleep disturbances and clinical symptoms: marked signs of Parkinson's disease was associated with a significant delay in the onset of sleep, prolonged waking periods and a reduction of light synchronous sleep. Long-term administration of L-DOPA caused an increase in rapid eye movement (REM) sleep as well as NREM sleep, corresponding with a marked improvement in the clinical symptoms of Parkinson's disease. This effect of L-DOPA on sleep is attributed to regained mobility. There is also a specific influence of L-DOPA on REM sleep, viz.,prolongation of REM latency with an REM rebound in the second half of the night. 47 references. (Author abstract modified)

195882 Cunningham, Constance Patricia Cayo. University of Texas at Austin **An exploratory study of the long term effects of drug use in hyperkinesis. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-5224 HC$12.50 MF$4.00 161 p.

The possibility that the long-term therapeutic use of drugs in the treatment of hyperkinetic children might result in effects which can be found and measured through the use of psychometric tests was investigated. A sample of 45 children 13 to 19 years old was drawn from the records of the Harry Jersig Speech and Hearing Center, San Antonio, Texas. Statistical analysis showed significant improvement on cognitive tests by subjects on calming drugs. Those on stimulant drugs showed losses, but not significant ones, and there was virtually no change in the no drug group on these measures. Length of time of drug use (both calming and stimulant) seemed to have an effect. Academic loss was not attributed to drug use, and scores on self-esteem measures were uniformly low for all groups. (Journal abstract modified)

195940 Klinger, A.; Satterfield, J.; Meisel, W. Computer Science Department, University of California, Los Angeles, CA **Pattern analysis of psychiatric research data.** Journal of Psychiatric Research (Oxford). 10(2):163-164, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,the multivariate statistical procedures which were employed in analyzing response patterns to questionnaires and psychological tests used in a psychiatric research project conducted at a clinic for hyperkinetic children were described. The main goal of the project was to define a measure of drug effectiveness and to described what differentiates behavior drug treated children from that of placebo treated patients by processing before treatment, after treatment, and difference data. It was found that pattern recognition techniques which were nonlinear and unconventional from the statistical point of view and which were being used for data analysis of both the teacher evaluations and psychological data were superior to the linear discriminant analysis technique, since they fit the type of data obtained from questionaires. 2 references. (Journal abstract modified)

196039 Angst, J.; Baumann, U.; Hippius, H.; Rothweiler, R. Psychiatrische Universitatsklinik, Postfach 68, CH-8029 Zurich, Switzerland **Clinical aspects of resistance to imipramine therapy.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 7(4):211-216, 1974.

The clinical aspects of resistance to imipramine therapy were examined in 92 patients suffering from endogenous depression. Responders and nonresponders to imipramine showed no difference in the psychopathological base level when measured by means of 12 scales of the AMP system; showed no sexual differences in the course of treatment; long-term patients and patients whose episode had been precipitated by psychological factors reacted more favorably under imipramine. Results were generally negative and the positive findings should be researched further. (Author abstract modified)

196600 Pakkenberg, H.; Fog, R. Dept. of Neurology, Kommunehospitalet, DK 1399, Copenhagen, Denmark **Spontaneous oral dyskinesia: results of treatment with tetrabenazine, pimozide, or both.** Archives of Neurology. 31(5):352-353, 1974.

Results of the treatment of spontaneous oral dyskinesia with tetrabenazine, pimozide or both are evaluated in 16 Ss. The most striking feature of the treatment by either drug is the rapid effect with almost total disappearance of the hyperkinesia in nearly all of the Ss. If the hyperkinesia reappears, the two drugs in combination are permanently efficient. 9 references. (Author abstract modified)

197137 Silverstone, Trevor. Psychiatry Dept., St. Bartholomew's Hospital, London **Intermittent treatment with anorectic drugs.** Practitioner (London). 1274(213):245-252, 1974.

The effectiveness of intermittent therapy with an anorectic drug when the drug is given first, as opposed to administration later on in the therapy, was investigated. The results show that intermittent medication with diethylpropion, provided that treatment begins with a period on the active drug, is as effective as continuous medication in the treatment of obesity. As there is likely to be less risk of development of any long-term dependence with intermittent medication, it is suggested that this type of regimen is suitable for those obese patients for whom anorectic drug therapy is considered advisable. 13 references.

197816 Guilleminault, Christian; Wilson, Richard A.; Dement, William C. Sleep Disorders Clinic and Laboratory, Stanford University School of Medicine, Stanford, CA 94305 **A study on cataplexy.** Archives of Neurology. 31(4):255-261, 1974.

Cataplexy, an abrupt and reversible paralysis was studied in 50 rapid eye movement (REM) sleep narcoleptics. During the attacks, lasting for a few seconds to 30 min, the EEG remained similar to the normal base line awake EEG recorded previously; there were short periods where REM sleep could not be eliminated. Electromyographic tracings recorded an abrupt drop in muscle tone during attacks but the numbers of muscles involved varied from one attack to another. Normal jerk reflexes could not be elicited and H-reflex was abolished. An exceptional patient with status cateplecticus with more than 30 daily cataplectic attacks was given levodopa, L-hydroxytryptophan and atropine sulfate in separate trials with no beneficial effect. Intravenously administered clomipramine hydrochloride suppressed the attacks dramatically. 37 references. (Author abstract modified)

197841 Munch-Petersen, S.; Pakkenberg, H.; Kornerup, H.; Ortmann, J.; Ipsen, E.; Jacobsen, P.; Simmelsgard, H. Sct. Hans Hospital, Roskilde, Denmark **RNA treatment of dementia: a double-blind study.** Acta Neurologica Scandinavica (Kobenhavn). 50(5):553-572, 1974.

A double-blind study of ribonucleic acid (RNA) treatment of dementia is presented. The material consisted of 22 mental hospital patients with mild to moderate degrees of dementia. Ten of these patients received treatment by oral administration of about 20 g hydrolyzed yeast RNA daily over a period of 4 months, while 12 patients received placebo. A psychological investigation and a clinical evaluation were performed prior to, during and immediately after the investiagion, as well as 2 months later. A neurological investigation, electroencephalographic determination of serum uric acid, serum creatinine and serum cholesterol were all made simultaneously with the psychological tests. Pneumoencephalography was performed in 12 patients prior to the start of the investigation (7 of these showed moderate, diffuse atrophy, and 5 showed severe, diffuse atrophy). It is concluded that there was no change in the state of dementia as a result of the treatment given. 21 references. (Author abstract modified)

198020 Wright, Logan; Craig, Shelley C. Dept. of Pediatrics, Children's Memorial Hospital, Univ. of Oklahoma Health Sciences Center, Oklahoma City, OK 73190 **A comparative study of amphetamine, ephedrine-atropine mixture, placebo and behavioral conditioning in the treatment of nocturnal enuresis.** Journal of the Oklahoma State Medical Association. 67(10):430-433, 1974.

Amphetamine, ephedrine - atropine mixture, placebo, and behavioral conditioning are comparatively studied in the treatment of nocturnal enuresis in 21 children between 4 and 10 years of age. Subjects were randomly assigned to receive either pad and bell conditioning or medication treatment. The conditioning group maintained a significant decrease in wettings per week after 4 weeks. The drug group showed an initial decrease in wettings which could not be maintained. This change was interpreted as primarily a placebo effect. 8 references. (Author abstract modified)

198074 Wittenborn, J. Richard. Rutgers University, New Brunswick, NJ **Responses of dysphoric patients to pharmacotherapies.** Psychopharmacology Bulletin. 10(2):54, 1974.

The effects of various drug treatments on dysphoric (retarded, depressed, anxious, and elated) patients are studied in an attempt to identify the optimal therapy for the individual patient. Patients received imipramine, thioridazine, or amitriptyline in a double-blind design which included administration of mood scales, tests of cognitive functioning, measures of perceptual performance, a psychosomatic inventory, and routine laboratory tests of physical parametors, as well as reports of doctors and nurses. Data show that regardless of medication, treatment is less than satisfactory in about one third of the patients. (Journal abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

193498 Wells, Brian. no address **Psychedelic drugs.** New York, Jason Aronson, 1973. 250 p. $10.00.

The dangers involved in the use of hallucinogenic drugs are discussed along with their potential benefits. Mescaline and cannabis are considered from the point of view of possible therapeutic uses. Areas examined include minor and major psychedelics, pathogenic aspects, sex and sexuality, psychedelic philosophy, crime and aggression, creativity, and religion.

193590 Harrison, Steadman Darnell, Jr. Indiana University **Chemical pharmacology of the benzo(b)thiophene and 1-methylindole analogs of N,N-dimethyltryptamine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, no 74-368 HC$12.50 MF$4.00 82 p.

A qualitative and quantitative comparison was made of the metabolism of N,N-dimethyltryptamine (DMT) and its 1-methylindole and benzo(b)thiophene analogs (DMT-1-Me and DMT-S) in vitro and in vivo in the rat liver. A consideration of the nuclear magnetic resonance and visible spectral characteristics of 6-hydroxytryptamine and its analogs allowed some speculation as to why hydroxylation occurs preferentially at the six position of these compounds. It can be argued that resonance stabilization of certain key intermediates may be responsible for lowering the energy barrier to hydroxylation at the six position..A McLafferty rearrangement apparently characteristic of all 3-(2-methylaminoethyl)indoles and their benzo(b)thiophene and 1-methylindole analogs was discovered in mass spectral studies of the metabolites of DMT-S and DMT-1-Me. The rearrangement also occurs in the primary amines and the corresponding tryptophols. These comparative mass spectral studies allow postulation of the origin of m/e 115, a fragment in the spectra of three substituted derivatives of indole, 1-methylindole, and benzo(b) thiophene. This fragment was previously thought to be unique to indoles. (Journal abstract modified)

194459 Murazaki, Mitsukuni. Department of Neuropsychiatry, School of Medicine, Kitazato University, Japan **Hallucinogen.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(5):514-526, 1974.

The literature on hallucinogens is reviewed. The psychiatric symptoms induced by LSD-25, cannabis sativa and organic solvents are considered. The possibilities of using these hallucinogens for treatment of psychiatric illness are also discussed. 56 references.

193028 Caldwell, John; Sever, Peter S. Department of Biochemistry, St. Mary's Hospital Medical School, London, England **The biochemical pharmacology of abused drugs: I. Amphetamines, cocaine, and LSD.** Clinical Pharmacology and Therapeutics. 16(4):625-638, 1974.

The drugs of dependence and their powerful central nervous system (CNS) actions are reviewed. The major central nervous system stimulants, amphetamine and cocaine, and the hallucinogen, lysergic acid diethylamide (LSD) are discussed. Cocaine is not of great significance in the current drug abuse scene due to its high cost (it is a plant product) and the difficulty in obtaining it. It now finds little application in medicine, so that it can rarely be obtained either by prescription or burglary of pharmacies. Its place has been taken by the amphetamines, most notably by methamphetamine (Speed); the amphetamines are readily available synthetic drugs. Cocaine and the amphetamines are popular with drug abusers seeking mood elevation. The appeal of LSD is the introverted who perhaps seek self-knowledge, and it has been used experimentally as an adjunct to psychotherapy of a range of mental disorders. 83 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

192943 Waldmeier, P. C.; Greengrass, P. M.; Maitre, L. Forschungsdepartement, Division Pharma, CIBY-GEIGY AG, 4002 Basel, Switzerland **Does maprotiline (LUDIOMIL) influence serotonin uptake and free tryptophan concentration in human plasma?** Experientia (Basel). 30(6):697, 1974.

At the Sixth Annual Meeting of the Union of Swiss Societies for Experimental Biology, the influence of maprotiline, a tetracyclic antidepressant, on plasma tryptophan binding, serotonin uptake and content of blood platelets in healthy volunteers was reported. No alteration in plasma tryptophan binding was noted after maprotiline treatment in contrast to a marked increase in free tryptophan in the acetylsalicylate group. Neither maprotiline nor acetylsalicylate had an influence in the uptake or content of serotonin in blood platelets from the samples. (Journal abstract modified)

193800 Ludin, H. P.; Robert, F. Neurologische Universitatsklinik, Inselspital, 3010 Bern, Switzerland **The action of diazepam on human skeletal muscle.** European Neurology (Basel). 11(6):345-352, 1974.

The action of diazepam on human skeletal muscle was investigated. In normal human Ss, the twitch force in the adductor pollicis muscle elicited by supramaximal stimulation of the ulnar nerve is significantly lowered by diazepam, whereas the tetanic force is not influenced. The evoked potentials recorded electromyographically from the same muscle are also not influenced by the compound. Decrease of the twitch force after supramaximal single stimulation of the nerve is most likely due to an action of diazepam on the muscle itself. There is no evidence for an action on the excitable membrane of the muscle. The effect is assumed to be part of the muscle relaxant activity of the compound in addition to the well known actions on the central nervous system. 10 references. (Author abstract modified)

194062 Boston Collaborative Drug Surveillance Program. 400 Totten Pond Rd., Waltham, MA 02154 **Reserpine and breast cancer.** Lancet (London) 2(7882):669-671, 1974.

The association between use of reserpine and breast cancer is revealed. Newly diagnosed cases of breast cancer and matched controlswere compared and it was found that the risk of breast cancer is over threefold in women exposed to reserpine compared with women not exposed. These results stimulate the collection of two other sets of data, both supporting the increase in breast cancer among reserpine users. Causality of the association is found to be a distinct possibility. 10 references. (Author abstract modified)

194063 Armstrong, Bruce; Stevens, Nancy; Doll, Richard. R.P.M. Dept., Radcliffe Infirmary, Oxford, 0X2 6PS, England **Retrospective study of the association between use of rauwolfia derivatives and breast cancer in English women.** Lancet (London). 2(7882):672-675, 1974.

The association between breast cancer and the use of rauwolfia derivatives is confirmed in a retrospective study of 708 breast cancer patients and 1430 control patients with other neoplasms. The use of rauwolfia was found significant statistically at the 5% level when other neoplasms previously suggested to be associated with reserpine use were removed from the control group. No association is found between breast cancer and the use of other hypotensive drugs or the use of other drugs known to enhance pituitary prolactin release. 6 references. (Author abstract modified)

194064 Heinonen, O. P.; Shapiro, S.; Tuominen, Liisas; Turunen, M. I. 400 Totten Pond Road, Waltham, MA 02154 **Reserpine use in relation to breast cancer.** Lancet (London). 2(7882):675-677, 1974.

The reserpine use in cases of newly diagnosed breast cancer and in controls admitted to the University Hospital, Helsinki, for elective surgery for benign conditions is investigated. Case - control pairs were matched for the year of operation (1960-72) and for half decade of age. A positive association between reserpine use and breast cancer was observed. Among 438 pairs, there were 68 that were discordant for reserpine use, with the drug being taken by the case in 45 pairs and by the control in 23. The association was most prominent in women admitted during 1970-72. 4 references. (Author abstract modified)

194065 no author. no address **Rauwolfia derivatives and cancer.** Lancet (London). 2(7882):701-702, 1974.

The use of rauwolfia derivatives in psychosis and hypertension is reviewed and its newly discovered relationship with breast cancer is discussed. Research studies from Oxford and Helsinki are compared with work in Boston. It is found that if rauwolfia is a risk factor in breast cancer, then a mechanism of induction which involves prolactin as a stimulator of mammary tumors in animals and man may be postulated. Reserpine is known to increase prolactin concentrations, probably by reducing hypothalamic monoamine activity which stimulates the release of prolactin inhibiting factor. It is noted that the role of prolactin in breast cancer is not fully established. It is found that the therapeutic advantages of rauwolfia do not outweigh the reported cancer risk.

194397 Rapoport, J.; Quinn, P.; Scribanu, N.; Murphy, D. L. Pediatrics, Georgetown University Hospital, Washington, DC 20007 **Platelet serotonin of hyperactive school age boys.** British Journal of Psychiatry (London). 125:138-140, 1974.

Platelet serotonin content was examined before and during treatment with methylphenidate and imipramine in a group of boys with the hyperactivity syndrome. Imipramine treatment markedly reduced platelet serotonin, while methylphenidate had no similar effects. As both drugs were clinically effective, it seems unlikely that change in serotonin transport or storage is closely related to the mechanism of actions of these drugs on hyperactive behavior. 12 references. (Author abstract modified)

194542 Chase, Thomas N.; Shoulson, Ira. Neurology Unit, NIMH, Bethesda, MD 20014 **Dopaminergic mechanisms in patients with extrapyramidal disease. (Unpublished paper).** Bethesda, Md., NIMH, 1974. 16 p.

Clinical studies of piribedil alone and in combination with pharmacologic agents which potentiate the motor effects of presumptive dopamine (DA) receptor agonists in the experimental animal are described. Human data indicate that piribedil exhibits several characteristics expected of a DA receptor stimulating agent. This piperonyl piperazine derivative appears to diminish central DA turnover, ameliorate the cardinal features of parkinsonism and reduce prolactin secretion. However, the therapeutic response of parkinsonian patients to piribedil is substantially less than to L-dopa. Its action as a partial DA receptor agonist might explain these results. Neither clonidine nor caffeine, which potentiate the ability of L-dopa or piribedil to induce hypermotility in rodents, enhanced the antiparkinsonian efficacy of piribedil. 31 references.

194826 Dorus, Elizabeth; Pandey, Ghanshayam N.; Frazer, Alan; Mendels, Joe. Research Dept., Illinois State Psychiatric Institute, 1601 W. Taylor, Chicago, IL 60612 **Genetic determinant of lithium ion distribution. I. An in vitro monozygotic-dizygotic twin study.** Archives of General Psychiatry. 31(4):463-465, 1974.

The possibility of a genetic determinant of lithium ion distribution was evaluated using a monozygotic (MZ) - dizygotic (DZ) twin study method. Red blood cell (RBC) lithium ion concentrations were assessed for ten MZ and seven DZ twin pairs following a 24 hour incubation in vitro. The distribution of intrapair difference scores of MZ twin pairs and DZ twin pairs were relatively nonoverlapping, with MZ intrapair difference scores being smaller on the average. A heritability index of 0.85, calculated as a function of intrapair difference scores, indicated that a substantial genetic factor is operative in RBC uptake of lithium ion. 19 references. (Author abstract modified)

194854 Model, D. G.; Berry, D. J. Edgware General Hospital, Edgware, Middlesex, England **Effects of chlordiazepoxide in respiratory failure due to chronic bronchitis.** Lancet (London). 2(7885):869-870, 1974.

The effect of normal oral doses of chlordiazepoxide was studied in a double-blind crossover trial in seven patients with respiratory failure due predominantly to chronic bronchitis. In six patients, the drug caused a highly significant increase in mixed venous carbon dioxide tension and a significant fall in forced expiratory volume in 1 sec. In three of these patients, serial plasma chlordiazepoxide levels were measured, and in two they were in the same range as in five nonbronchitic control patients. In the seventh patient, who was subsequently found to have taken a benzodiazepine tranquilizer regularly before the trial, chlordiazepoxide has no effect on the variables measured. Serial plasma chloridazepoxide levels in this man were in the same range as in the controls. It is concluded that chlordiazepoxide is contraindicated in patients with respiratory failure due predominantly to chronic bronchitis. 8 references. (Author abstract)

194857 Young, S. N.; Sourkes, T. L. Laboratory of Neurochemistry, Dept. of Psychiatry, McGill University, Montreal, Quebec H3A 1A1, Canada **Antidepressant action of tryptophan.** Lancet (London). 2(7885):897-898, 1974.

The action of tryptophan in the relief of depression is reviewed, noting several undesirable consequences to tryptophan therapy. Tryptophan metabolism in mammalian systems is discussed. It is noted that because of cortisol and substrate induction of tryptophan pyrrolase, when depressed patients are receiving large doses of tryptophan chronically,

the rate of tryptophan breakdown will be very greatly increased. The ensuing increase in tryptophan metabolites leads to a number of undesirable effects, including: 1) inhibition of gluconeogenesis; 2) increased deposition of hepatic triglycerides; 3) increased formation of possible carcinogens; and 4) effects on brain 5-hydroxytryptamine (5-HT). It is suggested that the doubtful efficacy of tryptophan as an antidepressant is due to its rapid breakdown. The consequences of tryptophan loading suggest that it would be beneficial to administer nicotinic acid with tryptophan to eliminate undesirable side-effects and prolong and increase the rise in brain 5-HT. 37 references.

195039 Serafetinides, E. A.; Willis, D.; Clark, M. L. VA Hospital, Brentwood, CA 90024 **The EEG effects of zinc in geriatric psychiatric patients.** International Pharmacopsychiatry (Basel). 9(2):95-99, 1974.

Electroencephalogram (EEG) studies were conducted in 24 geriatric men and women patients, hospitalized for psychiatric reasons, who participated in a double-blind, placebo controlled trial of zinc. It was found that medication was associated with no obvious EEG differences. Patients could be differentiated on the basis of slow rhythms present. It was found that great abundance of slow EEG rhythms was associated with mental deterioration of an organic type, whereas better scoring patients had more normal looking EEG. 11 references. (Author abstract)

195053 Hollister, Leo E.; Kanter, Saul L.; Board, Robert D.; Green, Donald E. VA Hospital, Palo Alto, CA 94304 **Marihuana metabolites in urine of man: III. Unchanged delta9-tetrahydrocannabinol.** Research Communications in Chemical Pathology and Pharmacology. 8(4):579-584, 1974.

Positive identification of unchanged delta9-tetrahydrocannabinol (THC) in the urine of man was made following single oral doses of 30mg in four subjects. Unchanged THC was found only in small amounts, approximately 0.01 - 0.005% of amount administered, and for only a few hours following drug administration. 10 references. (Author abstract)

195055 Gottschalk, Louis A.; Biener, Robert; Dinovo, Eugene C. Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA 92664 **Effect of oral and intramuscular routes of administration on serum chlordiazepoxide levels and the prediction of these levels from predrug fasting serum glucose concentrations.** Research Communications in Chemical Pathology and Pharmacology. 8(4):697-702, 1974.

The effects of oral and intramuscular routes of administration on serum chlordiazepoxide levels and the prediction of these levels from fasting predrug serum glucose concentrations is reported. Higher serum chlordiazepoxide levels were obtained after oral as compared to intramuscular administration of 25mg of chlordiazepoxide hydrochloride. Predrug fasting serum glucose levels predicted (by significant negative correlations) serum chlordiazepoxide levels 1 and 2 hours postdrug. 9 references. (Author abstract)

195445 Hillestad, L.; Hansen, T.; Melsom, H. Medical Departments, Sentralsykehuset, Akershus, Oslo, Norway **Diazepam metabolism in normal man: II. Serum concentration and clinical effect after oral administration and cumulation.** Clinical Pharmacology and Therapeutics. 16(3,Part1):485-489, 1974.

The serum concentration and clinical effect after oral administration and cumulation of diazepam were examined in man. Diazepam given orally over a period of days produces cumulation in the serum of diazepam as well as N-desmethyldiazepam. A balanced serum level is achieved at the end of the first week for diazepam, at the beginning of the second week for N-desmethyldiazepam, and from this time on it is higher than the mother substance. The biologic half-life of diazepam was found to be 54 hours, and the apparent biologic half-life of N-desmethyldiazepam, 92 hours. There was close correspondence between the serum levels of diazepam and its clinical effects. During continued administration over one to two weeks, some development of tolerance could be demonstrated. Cumulation of the metabolite was marked during continuous oral administration of diazepam, but clinical effects of the metabolite could not be demonstrated; effects seem to be related solely to serum levels of diazepam. 5 references. (Author abstract)

195446 Groth, Ulrich; Prellwitz, Winfried; Jahnchen, Eberhard. Zentrallabor de Medizinischen Kliniken und Pharmakolisches Institut, University of Mainz, Mainz, Germany **Estimation of pharmacokinetic parameters of lithium from saliva and urine.** Clinical Pharmacology and Therapeutics. 16(3,Part1):490-498, 1974.

The salivary and urinary excretion of lithium was studied in three healthy male subjects after oral administration of two or three different doses. In all individuals the concentration of lithium in salivary fluid was found to be 2.2to 3.3times as high as the concentration in plasma. In each subject the saliva:plasma concentration ratio remained constant over more than a 100 fold concentration range for at least 3 months. This ratio was not markedly affected by about tenfold changes in saliva flow rate. Pharmacokinetic parameters obtained from salivary excretion data are in agreement with those obtained from plasma concentration and urinary excretion rate data, and renal clearance of lithium can be estimated from salivary excretion data. Diurnal rhythms in the urinary excretion rate of lithium were observed. Thus, once the saliva:plasma concentration ratio is established (by taking only a few blood samples), the measurement of saliva concentrations should provide all pharmacokinetic information necessary for rational dosage regimens. 21 references. (Author abstract)

195447 Roth, Jerome A.; Gillis, C. N. Department of Anesthesiology, Yale University School of Medicine, New Haven, CT 06520 **Deamination of beta-phenylethylamine by monoamine oxidase -- inhibition by imipramine.** Biochemical Pharmacology (Oxford). 23(18):2537-2545, 1974.

The inhibition by imipramine of the deamination of beta-phenylethylamine by monoamine oxidase is reported. The oxidative deamination of tyramine (Tyr), 5-hydroxytryptamine (5-HT), and beta-phenylethylamine (PEA) by mitochondrial preparations of rabbit lung and brain was inhibited by imipramine. This tricyclic iminodibenzyl antidepressant drug was most effective in decreasing the deamination of PEA. Imipramine induced inhibition of monoamine oxidase (MAO) was shown to be of a mixed type based on Lineweaver-Burk plots, but was found to be completely reversible. The desmethyl and didesmethyl derivatives of imipramine were equally as effective as the parent drug in inhibiting the deamination of PEA, whereas the N-oxide analog of imipramine was less effective as an inhibitor of this reaction. These results support the premise that the action of imipramine as a clinically effective antidepressive agent may be related to its inhibitory effect on the specific form of MAO

which deaminates PEA. 28 references. (Author abstract modified)

195930 Frazer, A.; Wang, Y. C.; Pandey, G.; Mendels, J. Departments of Psychiatry and Pharmacology, University of Pennsylvania, Philadelphia, PA **Effect of monovalent cations on human platelet adenyl cyclase activity.** Journal of Psychiatric Research (Oxford). 10(2):156, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,a study which examined the possibility that lithium (Li) inhibits hormone induced stimulation of adenyl cyclase in various tissues was reported. Human platelets in which adenyl cyclase was stimulated by prostaglandin E(PGE) were used. It was found that the addition of increasing amounts of PGE produced a dose related increase in enzyme activity, that low concentrations of Li, sodium or potassium significantly reduced the stimulation of adenyl cyclase produced by PGE, and that the monovalent cations by themselves did not alter basal enzyme activity. (Journal abstract modified)

195949 White, Beverly J.; Driscoll, Edward J.; Tjio, Joe-Hin, Smilack, Zale H. Room 9D-08, Bldg. 10, National Institute of Arthritis, Metabolism, and Digestive Diseases, Bethesda, MD 20014 **Chromosomal aberration rates and intravenously given diazepam: a negative study.** Journal of the American Medical Association. 230(3):414-417, 1974.

The effects of intravenously given diazepam on human chromosomes in vivo were studied. Previous studies of the effects of diazepam (Valium) have given conflicting results. To resolve this problem chromosome analysis was on the peripheral blood of 20 healthy young adults, sampled both done before and after a single 12 to 20mg intravenous dose of diazepam. All subjects were oral surgery research patients of the National Institute of Dental Research. The mean percentages of chromosomal aberrations per person showed no significant increase during the immediate and 7 day period after use of the drug. While the experimental design of the study was complicated by the use of other drugs to control pain, it could be concluded that no genetic damage as measured by chromosomal analysis was detected following a single therapeutic dose of diazepam. 10 references. (Author abstract modified)

196087 Post, Robert M.; Goodwin, Frederick K. 3-West Clinical Research Unit, Section on Psychobiology, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Time-dependent effects of phenothiazines on dopamine turnover in psychiatric patients. (Unpublished paper).** Bethesda, Md., NIMH, 1974. 9 p.

The dependent effects of phenothiazines on dopamine turnover were examined in psychiatric patients. Ss treated with chlorpromazine and thioridazine for less than 3 weeks demonstrated elevated probenecid induced accumulations of homovanillic acid (HVA), a major dopamine metabolite, in cerebrospinal fluid. After more than 3 weeks treatment, HVA accumulations were no longer elevated. This suggests that the effects of phenothiazines on dopamine turnover are time dependent; they may reflect a centrally mediated tolerance and may be related to the time course of antipsychotic efficacy. 25 references. (Author abstract modified)

196188 Birnbaum, D.; Karmeli, F. Gastroenterological Service, Hadassah University Hospital, Jerusalem, Israel **The effect of psychopharmaca on uropeptic activity.** Psychotherapy and Psychosomatics (Basel). 24(2-3):102-105, 1974.

Various psychopharmaca were studied with regard to their effect on uropepsin secretion in rats and humans. It was found that these drugs markedly inhibited uropepsin secretion, especially etumine and melleril derivatives. In humans, uropeptic activity following diazepam and melleril, was similar to that observed in patients who underwent vagotomy. These observations on uropepsin secretion are in accord with the observed inhibition of gastric secretion following peroral or parenteral administration of diazepam and mesoridazine. 8 references. (Author abstract)

196260 Wang, Yao Chun. University of Pennsylvania **Depressive illness: adrenergic responsiveness and the effect of lithium on platelet adenyl cyclase. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-2477 HC$12.50 MF$4.00 146 p.

Central adrenergic responsiveness in depressive illness was investigated via measuring a peripheral response to norepinephrine (NE) in moderately depressed male patients and normal controls. Platelet adenyl cyclase was used, since it had been considered to be the receptor or part of the receptor system for catecholamines. The production of radioactive cyclic-AMP in intact platelets, previously incubated with H3-adenine was used as an index of adenyl cyclase activity. Prostaglandin E1(PGE1) was used to stimulate enzyme activity, and the inhibitory effect of NE on PGE1 stimulated activity was evaluated. The effect of lithium (Li) on the stimulation of adenyl cyclase by PGE1 was also analyzed. The effects of raising the magnesium (Mg)tration during the labeling incubation were also investigated, and data suggest that the inhibitory effect of Li on hormone stimulated adenyl cyclase may result from its competing with Mg for some stimulatory site of the enzyme. (Journal abstract modified)

196836 Horst, W. Dale; Spirt, Nena. Department of Pharmacology, Hoffman-La Roche, Inc., Nutley, NJ 07110 **A possible mechanism for the anti-depressant activity of thyrotropin releasing hormone.** Life Sciences. 15(6):1073-1082, 1974.

L-pyroglutamyl-L-histidyl-L-proline-amide (TRH), a thyrotropic releasing hormone, has been found to cause an increase in the release and turnover of norepinephrine in rat brain tissue while having no effect on the endogenous levels of this amine. TRH did not influence the uptake of norepinephrine by brain tissue. The release of norepinephrine by TRH may be the mechanism whereby TRH reverses mental depression. 26 references. (Author abstract)

196926 Hilton, Barbara P. Dept. of Neurochemistry, Institute of Neurology, National Hospital, Queen Square, London, England **Effects of reserpine and chlorpromazine on 5-hydroxytryptamine uptake of platelets from migrainous and control subjects.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 37(6):711-714, 1974.

Discrepancies between the uptake of 5-hydroxytryptamine (5-HT) by platelets of migrainous and control subjects were studied and platelet aggregation experiments confirmed differences between the 5-HT receptors of migrainous and control platelets. However, no differences were found in 5-HT uptake, in the presence of reserpine or chlorpromazine, into migrainous and control platelets. The results support the hypothesis that receptors for 5-HT induced platelet aggregation provide a model for vascular receptors causing constriction and are distinct from those transferring 5-HT through the platelet membrane. 10 references. (Author abstract modified)

197459 Babington, R. G.; Horovitz, Z. P. Department of Pharmacology, E. R. Squibb and Sons, Inc., Princeton, NJ **Neuropharmacology of SQ 10,996, a compound with several therapeutic indications.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 202(1):106-118, 1973.

A neuropharmacologic profile of SQ 10996 which suggests that it is a compound with several possible clinical applications is presented. SQ 10996 compared favorably with carbamazepine and diphenylhydantoin in tests designed to predict antiepileptic activity. Similarly, SQ 10996 and carbamazepine were quite active in testing to delineate effectiveness in the treatment of trigeminal neuralgia. The most promising laboratory findings were that SQ 10996 possesses possible antidepressive and antianxiety activities. 30 references. (Author abstract)

197831 Boyd, A. E., III.; Mager, M.; Angoff, G.; Lebovitz, H. E. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760 **Effect of acute administration of L-dopa on body temperature in man.** Journal of Applied Physiology. 37(5):675-678, 1974.

The effect of L-di-hydroxyphenylalanine (L-dopa), a precursor of the catecholamines norepinephrine and dopamine, on rectal temperature (Tre) and plasma growth hormone was studied in 24 young males. After oral administration of 0.5and 1.0g of L-dopa at 22 degrees C, Tre decreased significantly in 10 men, with a mean nadir of -.34 degrees C at the higher dose. Although plasma growth hormone increased in 22 of 24 men there was not correlation between the growth hormone rise and the decrease in Tre. Since monitoring of skin temperature did not indicate increased heat loss to the environment and since a decrease in Tre was also noted at a thermoneutral temperature, it would appear that L-dopa can decrease heat production in man. 26 references. (Author abstract modified)

197862 Adler, R.; Gervasi, A.; Holzer, B.; Hemmeler, W. Department of Medicine, University of Berne, Inselspital, CH-3010 Berne, Switzerland **Mild analgesics evaluated with the 'submaximum effort tourniquet technique': II. The influence of a tranquillizer on their effect.** Psychopharmacologia (Berlin). 38(4):357-362, 1974.

The influence of a tranquillizer on the effects of mild analgesics evaluated with the submaximum effort tourniquet technique. Using the submaximum effort tourniquet technique mild analgesics were better discriminated from placebo by subjects, demonstrating a calm behavior in the test situation than by individuals with prominent arousal reactions. A tranquilizer (benzoctadiene) was given in order to induce relaxation, with the aim to enhance the subjects ability to discriminate analgesics from placebo. Pain tolerance times in the six groups (placebo, C-44'328-Ba, paracetamol, alone, or in combination with benzoctadiene) on the four pain levels slight, moderate, severe and unbearable were not significantly different when compared by means of analysis of variance. The comparison of the groups showed that the combination of the analgesics with benzoctadiene was more effective than either analgesic given alone. In the non benzoctadiene group the analgesics were not differentiated from the placebo. Within the benzoctadiene group each analgesic was more effective than placebo on two pain levels. 11 references. (Author abstract modified)

197951 Klotz, U.; Avant, G. R.; Hoyumpa, A.; Schenker, S.; Wilkinson, G. R. Dr. Margarete Fischer-Bosch Institut fur Klinische Pharmakologie, D7 Stuttgart 50, Auerbachstrasse 112, Germany **Pharmacokinetics of diazepam in man.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282 (Supplement):R48, 1974.

At the 1974 meeting of the German Pharmacological Society, the pharmacokinetics of diazepam (D) after a single i.v. injection and/or oral administration was reported in 33 patients of various ages. With increasing age there was a significant increase of the terminal half-life (T1/2). T1/2 was 30.6hr in the younger patients, 47.1in the medium age patients and 75.8in the older patients. The prolongation of T1/2 could be correlated to an increase in the volume of distribution Vd(ss) and was further enhanced in the older patients by a reduction in total plasma clearance. D was rapidly absorbed with peak levels being present in 1 hour. The systemic availability was about 75%. (Journal abstract modified)

197956 Leopold, G.; Hameister, W.; Wahlig, H. Medical Research, E. Merck, D-61 Darmstadt, Frankfurter Strasse 250, Germany **The effect of bedrest and of physical activity on the blood level of Gentamycin after intramuscular application.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R57, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of bedrest and of physical activity on the blood level of Gentamycin after intramuscular application was reported. In bedridden patients the maximal serum concentrations of Gentamycin was lower and reached later than in patients under physical activity. (Journal abstract modified)

197976 Wagner, P.; Bader, H. Abteilung Pharmakologie, Universitat Ulm, D79 Ulm, Oberer Eselsberg, Germany **Effect of alcohols, chlorpromazine and diphenylhydantoin on (Ca2+)-ATPase of human red blood cells.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 282(Supplement):R103, 1974.

At the 1974 meeting of the German Pharmacological Society, the effect of alcohols, chlorpromazine and diphenylhydantoin on Ca2+-adenosine triphosphate-ase (ATPase) of human red blood cells were examined. The alcohols methanol, ethanol and n-propanol activiated both (Ca2+)-ATPases of human red cells at low concentrations and inhibited them at higher concentrations. The activation of the low affinity (Ca2+)-ATPase was about 30% for all three alcohols tested. The high affinity (Ca2+)-ATPase was maximal 90% activated by these alcohols at two times higher concentrations. Half maximal inhibition by the three alcohols was reached at 10 fold concentration of activation. Chlorpromazine increased the activity of the low affinity (Ca2+)-ATPase 9% and the activity of the high affinity (Ca2+)-ATPase 12%. (Journal abstract modified)

197992 Lieb, J.; Sclabassi, R.; Crandall, P.; Buchness, R. Department of Anatomy, School of Medicine, University of California, Los Angeles, CA 90024 **Comparison of the action of diazepam and phenobarbital using EEG-derived power spectra obtained from temporal lobe epileptics.** Neuropharmacology (Oxford). 13(8):769-783, 1974.

The action of the anticonvulsant drugs diazepam and phenobarbital on the electrical activity of temporal lobe structures was analyzed. Data are reported from six patients with intractable temporal lobe epilepsy in whom medication had failed to control seizures and in whom recording electrodes had been implanted in order to localize the more epileptogenic hemisphere with a view to therapeutic surgery. The effect of intravenous administration of these drugs on the electroencephalogram (EEG) was measured by means of the power spectrum, computed from EEG segments obtained both before and after the administration of the drugs. Diazepam was found to have striking, though varied, effects across the six patients.

There was a general tendency for diazepam to suppress activity in the lower frequency bands and to produce enhancement in the higher frequency bands. 32 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

193851 Bond, Alyson; Lader, Malcolm. no address **The use of analogue scales in rating subjective feelings.** British Journal of Medical Psychology (London). 47(3):211-218, 1974.

A series of 16 visual analog scales measuring subjective feelings was administered to 500 normal Ss and the results were subjected to a factor analysis using a principal component solution and orthogonal rotation of the factor matrix. Three factors were extracted: alertness, contentedness, and calmness. The scale was tested in an experiment designed to test the residual effects of butobarbitone sodium 150mg and flurazepam 15mg and 30mg, compared with a placebo. Although the first factor failed to reach statistical significance, it did show a trend in a meaningful direction and the other two factors showed clear drug effects. The three factors extracted by the factor analysis do seem to provide useful and meaningful data, and the mood rating scale has been sensitive enough to detect the residual effects of drugs taken 12-18 hours before. 9 references.

194655 Baxley, Gladys Bright. University of Kansas **Effects of psychotropic drugs on the short-term memory of retarded children. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-12524 HC$12.50 MF$4.00 154 p.

The effects of psychotropic drugs on the short-term memory of retarded children were investigated. Although there were some individual differences, different dosage levels of methylphenidate generally produced no apparent changes in the performance of each subject on either experimental task (recall of series of instructions and digits). Considering slight individual differences, methylphenidate and thioridazine produced the same effects as no drug on the ability of the Ss to acquire and maintain skill in performing increasingly more complex series of instructions and digits. (Journal abstract modified)

194827 Hollister, Leo E.; Berger, Philip; Ogle, Floradell L.; Arnold, Roger C.; Johnson, August. 3801 Miranda Ave., Palo Alto, CA 94304 **Protirelin (TRH) in depression.** Archives of General Psychiatry. 31(4):468-470, 1974.

Protirelin (thyrotrophin releasing hormone (TRH)) was evaluated as a treatment in depression in two independent investigations using a similar protocol. The latter was designed so that some patients received three 600 micro g intravenous injections of protirelin early in their course and others received them toward the end of their course of treatment. Regardless of when protirelin was given in the course of depression, or how the course of the illness was measured, it seemed to be devoid both of therapeutic and of major adverse effects. 5 references. (Author abstract)

194865 Salzman, Carl; Kochansky, Gerald E.; Shader, Richard I.; Porrino, Linda J.; Harmatz, Jerold S.; Swett, Chester P., Jr. Psychopharmacology Research Laboratory, Massachusetts Mental Health Center, 74 Fenwood Rd., Boston, MA 02115 **Chlordiazepoxide-induced hostility in a small group setting.** Archives of General Psychiatry. 31(3):401-405, 1974.

A small group model was used to examine the effects of chlordiazepoxide hydrochloride on affective and behavioral hostility in a social interactive setting. Three person groups of male volunteers completed paper and pencil affective rating scales individually and interacted with each other during a 10 minute discussion period that was videotaped and scored for behavioral hostility. The results indicated that chlordiazepoxide was associated with an increase in individual affective but not behavioral hostility. However, when a frustration stimulus was presented to the group, interpersonal behavioral hostility was increased in those who received chlordiazepoxide as compared with those taking a placebo. The data suggest that increases in hostility may be a regular rather than paradoxical effect of chlordiazepoxide. However, overt hostility may only become apparent in settings of interpersonal frustration. 44 references. (Author abstract)

195145 Stix, Allen Howard. University of Pittsburgh **A controlled series of experiments investigating some sociological effects of two dosages of chlordiazepoxide (Librium) upon individuals and small groups. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-18407 HC$12.50 MF$4.00 298 p.

The effects of chlordiazepoxide (Librium) on subjects' sociological behavior was studied during three experimental routines: 50 plays of the Prisoner's Dilemma game, a persuasion routine devised by Kurt Lewin, and the procedure devised by Robert Bales to study role differentiation and social structure in small, informal, task oriented groups. During the Prisoner's Dilemma game, the Librium group appeared to be more rational, played the game more cooperatively, and derived payments in significant excess of those won by the non-Librium groups. Data from the Lewinean routine unequivocally demonstrate that the Librium rendered subjects less susceptible to persuasion designed to produce private conformity while not concomitantly making them less responsive to group generated norms. During the Balesian routine, the Librium groups showed less of the behaviors of tension release, showing agreement, and providing suggestions and more of the behaviors of seeking orientation and showing tension and antagonism than the non-Librium groups. (Journal abstract modified)

195601 Walsh, Arthur C.; Walsh, Bernice H. 121 University Place, Pittsburgh, PA 15213 **Presenile dementia: further experience with an anticoagulant-psychotherapy regimen.** Journal of the American Geriatrics Soceity. 2(10):467-472, 1974.

The principles of an anticoagulant psychotherapy regimen for presenile dementia are discussed. Short histories are given of 10 patients (including one with Huntington's chorea as well as dementia) who responded well to this treatment. The importance of keeping the blood prothrombin time at 2.0-2.5times the control time is noted. The earlier the treatment is started, the better the result. Even in cases in which there is no significant improvement, the prevention of further deterioration is of great value. If properly controlled, this regimen is relatively safe and can maintain or improve the quality of life for dementia patients. 16 references. (Author abstract)

195773 Seedat, Y. K. Dept. Of Medicine, Univ. of Natal, Durban, Republic of South Africa **Prindolol in the management of hypertension.** New Zealand Medical Journal (Dunedin). 79(515):945-946, 1974.

Clinical experiences with various hypotensive drugs are discussed, including the use of thiazides, reserpine, and beta-adrenergic blockers such as propranolol and prindolol. Con-

siderations concerning beta-adrenergic blocking drugs are the length of time (2 to 3 weeks) to produce the desired blood pressure drop, the lesser therapeutic effect of these drugs upon diastolic blood pressures greater than 130mm Hg, and their failure with patients with increased blood urea.

195923 Feinberg, I.; Hibi, S. Veterns Administration Hospital, San Francisco, CA **Some amphetamine effects on REM sleep.** Journal of Psychiatric Research (Oxford). 10(2):151-152, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,research investigating whether the administration of dextroamphetamine (DA) causes a reduction in REM sleep and whether withdrawal after prolonged administration produces elevated REM levels (rebounds) was described. Four children with minimal brain dysfunction syndrome (MBDS) who were receiving long-term treatment with dosages of 5-60mg of DA or methylphenidate daily were studied. It was concluded that REM rebound does not invariably occur upon withdrawal after prolonged administration of amphetamines even when REM sleep had been depressed by the drug, and that an increase in dosage prior to withdrawal may be an important factor in producing REM rebound. It was also concluded that increased REM latency need not be associated with a decrease in total REM sleep, nor need the converse of this assumption be true. (Journal abstract modified)

196090 Singh, Gurmeet; Verma, H. C. Dept. of Psychiatry, Medical College, V. J. Hospital, India **Drug treatment of chronic intractable pain in patients referred to a psychiatry clinic.** Journal of the Indian Medical Association (Calcutta). 56(11):341-345, 1971.

Two antidepressants and a tranquilizer were tested in a controlled trial with 60 patients with chronic intractable pain. Ss were allocated to one of three treatment groups: chlordiazepoxide, amitriptyline, and imipramine. On chlordiazepoxide, only two of 20 Ss gave a good response in contrast to 16 out of 20 Ss who showed good response with both amitriptyline and imipramine. There was no significant difference in response between the latter two drugs. Later, 15 of the 18 chlordiazepoxide failures showed good response when treated with the antidepressant drugs. The Ss' other symptoms, such as anxiety, nervousness, palpitation, insomnia and fatigue also responded better to the antidepressant than to the tranquilizers. The response to antidepressants was better than to chlordiazepoxide, irrespective of whether Ss were diagnosed as suffering from anxiety, depression or pain without any psychiatric symptoms. It is suggested that the cases may constitute a single clinical entity in which pain is the presenting symptom of an underlying depression. 13 references. (Author abstract modified)

196146 Hattori, Takao. Department of Neuropsychiatry, Koritsu-Tosei Hospital, Aichi, Japan **Seizures of choreoathetic type induced by sudden movement: correlation to the biogenic amines.** Clinical Psychiatry (Tokyo). 16(4):379-385, 1974.

A case of choreoathetosis like involuntary kinesthetic seizure is discussed. The patient experienced convulsion of the right thigh while running at 9 years old, which lasted for a few seconds and disappeared by itself. He then experienced stronger and more generalized convulsion at every sudden physical movement. One second before each convulsion he had sense of onset of convulsion with the feeling of fear. He could avoid convulsion by stopping physical movement for 10 seconds when he had the sense of its onset. The EEG showed generalized paroxysmal abnormality, and a slight expansion of the left ventricle was observed. This convulsion remarkably decreased through treatment with haloperidol, was aggravated by L-DOPA, but completely disappeared after treatment with diphenylhydantoin. The patient seemed to have hypersensitivity of the dopaminergic system at the corpus striatum, and a temporal malfunction of the thalamus due to sudden movement facilitated dopamine metabolism, causing this convulsion. 25 references.

196197 Knobel, Mauricio. Dept. of Psychiatry, School of Medicine, Univ. of Buenos Aires, Larrea 1381, 2 Piso, Buenos Aires, Argentina **The use of trazodone in psychosomatic medicine.** Psychotherapy and Psychosomatics (Basel). 24(2-3):141-145, 1974.

A new antidepressant, a hydrochloride derivative of triazolpiridine or Trazodone, was tested. The previously proved low toxicity, tranquilizing and antidepressive effects of this product, led to its testing in psychosomatic diseases, where the depressive component was demonstrated. A group of 100 'somatic' patients who showed depressive signs on the Hamilton Rating Scale for Depression were submitted to Trazodone or placebo, following the double-blind technique. Considerations on the relationship between somatic disorders and depressive states are presented in order to explain the positive results obtained. 15 references. (Author abstract modified)

196443 Murasaki, Mitsukuni; Sato, Kiichiro; Mochizuki, Yasunori; Sugawara, Michiya; Hara, Toshio. Department of Psychiatry and Neurology, Kitasato University School of Medicine, Japan **Clinical evaluation of new anti-depressant, Lopramine.** Clinical Psychiatry (Tokyo). 16(4):409-411, 1974.

The effect of Lopramine (DB-2182) on depression was studied in an experiment in which 26 patients with depressive illness, five patients with presenile or senile depression, 18 patients with neurosis and seven with other (unidentified) depressive states were treated with this drug with or without minor tranquilizers, neuroleptics and sleeping pills. Lopramine was effective in 85.7% of the patients, notably in depressive illness within 7 to 14 days of beginning of treatment. Side-effects included dry mouth, constipation, fatigue, insomnia, excitation, vertigo, orthostatische, dysuria, edema, tachycardia and articulatory disturbance. 5 references.

196676 Howard, James S., III. Eastern State Hospital, Williamsburg, VA 23185 **Haloperidol for chronically hospitalized psychotics: a double-blind comparison with thiothixene and placebo: a follow-up open evaluation.** Diseases of the Nervous System. 35(10):458-463, 1974.

A study designed to compare haloperidol's effects on the signs and symptoms of psychosis and its propensity to induce side-effects with those of thiothixene, another potent, nonphenothiazine neuroleptic with low sedating properties and with those of placebo is reported. Forty six female patients, primarily schizophrenics, participated in the study. The patients given thiothixene either responded maximally and quickly or they did not respond at all. This was reflected by the drug's inability to significantly reduce the severity of any of the target symptoms measured in those patients not discharged from the hospital. Haloperidol produced a prompt and maximal response in an even greater proportion of patients than did thiothixene, and also produced a reduction in the severity of six of the 12 items measured in patients not discharged from the hospital. In all but one of the items measured, the results favored treatment with haloperidol. It is concluded that haloperidol is a safe, effective agent for use in the rehabilitation of chronically hospitalized psychotics. 13 references. (Author abstract modified)

196958 Bancroft, John; Tennent, Gavin; Loucas, Kypros; Cass, James. Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, OX3 7JX, England **The control of deviant sexual behaviour by drugs: I. Behavioural changes following oestrogens and anti-androgens.** British Journal of Psychiatry (London). 125(September):310-315, 1974.

The effects of cyproterone acetate and ethinyl estradiol on sexual behavior of sexual offenders was assessed using a combination of behavioral, attitudinal, and physiological measures. There was no significant difference between the drugs on any measure. They were equally effective in reducing frequency of sexual thoughts and sexual activity, whereas only cyproterone acetate produced a weak effect in reducing erectile and subjective response to erotic stimuli. The possibility of a placebo effect cannot be excluded. On the dosages used, neither drug produced troublesome side-effects. Further work is advocated to assess the effects of longer administration and varying dose levels. 23 references. (Author abstract)

197861 Adler, R.; Lomazzi, F. Department of Medicine, University of Berne, Inselspital CH-3010, Berne, Switzerland **Mild analgesics evaluated with the 'submaximum effort tourniquet technique'. I. The influence of psychological factors on their effect.** Psychopharmacologia (Berlin). 38(4):351-356, 1974.

The influence of psychological factors on the effects of mild analgesics evaluated with the submaximum effort tourniquet technique were examined. When the effects of placebo, C-44'328-Ba1 and Dextropropoxyphene were assessed by means of this method in 30 healthy male volunteers in a double-blind, crossover trial, the overall analysis of variance failed to show significant group differences. When psychological factors, i.e. level of anxiety, use of coping behavior in order to get distracted from pain, and style of relating to the experimenter (assessed by rating of interviews) were taken into account, the calm group with low levels of anxiety, low use of coping behavior and relaxed manner of relating, showed a trend toward better discrimination between placebo and analgesics than the aroused group. In the two extreme groups and most aroused, the response to the individual four trials was significantly different. The assumption of Beecher, that high levels of anxiety are neccessary for the experimental testing of analgesics seems to be correct for the group of narcotics, while for mild analgesics the best experimental situation might be one which permits the subject to remain calm and relaxed. 11 references. (Author abstract modified)

197867 Karniol, Isac G.; Shirakawa, Itiro; Kasinski, Nelson; Pfeferman, Abraham; Carlini, Elisaldo A. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu 862, 04023 Sao Paulo, Brazil **Cannabidiol interferes with the effects of delta9-tetrahydrocannabinol in man.** European Journal of Pharmacology (Amsterdam) 28(1):172-177, 1974.

The interaction between cannabidiol (CBD) and delta9-tetrahydrocannabinol (THC) in human beings was studied. In a double-blind procedure, 40 healthy male volunteers were assigned to 1 of 8 experimental groups, receiving by oral route, placebo, 30mg THC, 15, 30 or 60mg of CBD, and mixtures of 30 mg of THC plus either 15, 30 or 60mg of CBD respectively. Pulse rate, time production tasks and psycholocial reactions were measured at several time intervals after drug ingestion. 30mg THC alone increased pulse rate, disturbed time tasks and induced strong psychological reactions in the subjects. 15mg-60mg of CBD alone provoked no effects. CBD was efficient in blocking most of the effects of THC when both drugs were given together. CBD also decreased the anxiety component of THC effects, in such a way that the subjects reported more pleasurable effects. 22 references. (Author abstract modified)

198030 Jasinski, Donald R.; Nutt, John G.; Griffith, John D. National Institute on Drug Abuse, HEW, Lexington, KY **Effects of diethylpropion and d-amphetamine after subcutaneous and oral administration.** Clinical Pharmacology and Therapeutics. 16(4):645-652, 1974.

The effects of diethylpropion were determined and compared with those of d-amphetamine in nine subjects using a crossover design. Diethylpropion produced effects qualitatively similar to those of d-amphetamine, but significantly less potent. Orally diethylpropion was 1/6 to 1/11 as potent as d-amphetamine while subcutaneously diethylpropion was 1/10 to 1/20 as potent as d-amphetamine. A striking difference between diethylpropion and d-amphetamine was the relatively greater oral efficacy of diethylpropion. Diethylpropion was twice as potent orally as subcutaneously while oral and subcutaneous d-amphetamine were equipotent. 21 references. (Author abstract)

198045 Gittelman-Klein, Rachel. Long Island Jewish-Hillside Medical Center, Hillside Division, Glen Oaks, NY **Methylphenidate effects in learning disabilities of children.** Psychopharmacology Bulletin. 10(2):10, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which reported the effects of methylphenidate on the intellectual functioning of children who are free of behavioral deviance but who lag behind in learning. The subjects were randomly assigned to methylphenidate or placebo for a 12 week period. On the Wide Range Achievement Test (WRAT), both reading and arithmetic scores were significantly improved after 4 weeks of methylphenidate treatment. After 12 weeks of treatment, the methylphenidate and placebo groups were no longer significantly different either on the reading or arithmetic scores of the WRAT. The Gray Oral Reading Test was not sensitive to drug effect at any point. (Journal abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

193039 Kline, Nathan S.; Alexander, Stewart F.; Chamberlain, Ampara. no address **Psychotropic drugs: a manual for emergency management of overdosage.** Oradell, N.J., Medical Economics, 1974. 135 p.

Clear instructions are provided to identify the major clinical signs of psychoactive drug overdosage and to treat the major complications. One hundred twenty four compounds, listed alphabetically, have a color coded cross reference. A photo identification section makes it possible to identify exactly the medication ingested. A list of telephone numbers and locations of poison control centers throughout the U.S. is included.

193072 Swett, Chester, Jr. Boston Collaborative Drug Surveillance Program, 400 Totten Pond Rd., Waltham, MA 02154 **Drowsiness due to chlorpromazine in relation to cigarette smoking: a report from the Boston Collaborative Drug Surveillance Program.** Archives of General Psychiatry. 31(2):211-213, 1974.

The frequency of drowsiness attributed to orally administered chlorpromazine hydrochloride was compared among 130 nonsmokers and 201 'light' and 72 'heavy' cigarette smokers. Drowsiness occurred in 16%, 11%, and 3%, respectively. More rapid metabolism of chlorpromazine in cigarette smokers may explain these findings. 9 references. (Author abstract)

193087 Palatucci, Donald M. Neurodiagnostic Laboratory, 2001 Union St., San Francisco, CA 94123 **Iatrogenic dyskinesia: a unique reaction to parenteral methylphenidate.** Journal of Nervous and Mental Disease. 159(1):73-76, 1974.

An unusual side-effect occurring after i.v. injection of methylphenidate hydrochloride (Ritalin) in a patient with acute brain syndrome is reported. The patient, given 40mg of methylphenidate, developed a severe dyskinetic reaction. Similar dyskinesias have been reported in rare instances in patients who have taken oral methylphenidate, but never previously in a patient who was given the drug intravenously. Some implications of this unique occurrence are discussed. 8 references. (Author abstract)

193828 Kurioka, Yoshiyuki Hanna Sanatorium, Japan **A case of 'phenothiazine ileus' recovered from shock.** Clinical Psychiatry (Tokyo). 14(6):567-571, 1972.

The only case of 'phenothiazine ileus' recovered from shock is reported. Eight other cases have been reported, but none of the patients survived the shock. The patient in this case was a 37-year-old male diagnosed as a schizophrenic who had been in and out of mental hospitals over a period of more than 7 years. Except when his fever was high, he was treated with 200mg of chlorpromazine and 100mg of prometazine. The medical workup was normal, but ileus was suspected. The patient went into shock, with stoppage of his heartbeat and breathing, while undergoing X-ray examination in the sitting position. He was revived by artificial resuscitation. The shock was closely related to frequent vomiting and is believed to have been the result of severe dehydration and acute loss of electrolytes. Study of other reported cases definitely reveal the relationship between phenothiazine and paralytic ileus. Thus, this type of ileus should be called 'phenothiazine ileus.'In this particular case, the patient recovered from paralytic ileus after administration of chlorpromazine was stopped and he was infused to replace fluid, and by compensating for the lost electrolyte. 14 references.

193986 Munjack, Dennis; Razani, Javad. Dept. of Psychiatry, L.A. County-U.S.C. Medical Ctr., Psychiatric Out-Patient Clinic, Los Angeles, CA 90033 **Side effects of brevital-aided desensitization: some clinical impressions.** Behavior Therapy. 5(3):423-427, 1974.

The side-effects encountered with the intravenous administration of methohexital sodium (Brevital) using a maximum of 60 mg during 1 hr treatment sessions, are reported for 17 neurotic patients treated with Brevital aided desensitization. It is concluded, that while side-effects are moderately common, they are so mild as to pose no significant treatment obstacle. The drug is sufficiently safe, at low dosages, to allow in vivo treatment with rapid reexposure to anxiety eliciting stimuli without causing the patient undue distress. 17 references. (Author abstract)

194274 Varma, L. P. Ranchi Mansik Arogyashala, Kanke, Bihar, India **Drugs in psychiatry.** Journal of the Indian Medical Association (Calcutta). 56(5):128-134, 1971.

The characteristics and properties of the psychotherapeutic drugs Rauwolfia serpentina, chlorpromazine hydrochloride, triflupromazine hydrochloride, prochlorperazine, thioridazine, trifluoperazine, thioproperazine, and fluphenazine enanthate are discussed. Precautions, side-effects, and toxic reactions to these drugs are given, and the responsibility of the general practitioner in relation to these drugs is discussed. 11 references.

194511 Ambrosino, Salvatore V. Dept. of Clinical Psychiatry, School of Medicine, State University of New York, Stony Brook, NY **Depressive reactions associated with reserpine.** New York State Journal of Medicine. 74(5):860-864, 1974.

Five case studies of depression aggravated by reserpine are presented. There is ample evidence that these patients were anxious or depressed before the use of reserpine and that reserpine may have been used unknowingly to treat symptoms and signs of agitated depression, such as elevated systolic pressure. The continued use of the medication in a vulnerable population appears to aggravate an already existing condition by removing a major defense activity or work. The use of an activating type of antidepressant such as desipramine is recommended. 21 references.

194573 Aleksandrowicz, Malca Kroll. University of Kansas **Neonatal behavioral patterns and their relation to obstetrical medication. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-12516 HC$12.50 MF$4.00 207 p.

Neonate behavioral patterns and their relation to obstetrical medication were investigated. Analysis of behavior scores indicated consistent patterns of intercorrelation demonstrated by clustering around the following factors: orientation, responsivity to visual and auditory stimuli, habituation to visual and auditory stimuli during sleep, motor organization, state control, and excitability. The organization of behavior increased toward the end of the first month. The behavioral patterns were significantly affected by obstetrical drugs and some effects of general anesthesia, narcotics and tranquilizers persist at the age of 1 month. The most pronounced and diffuse effects were associated with general anesthesia and by combinations of potent narcotics with narcotic potentiating drugs (meperidine - promethazine or fentanyl - droperidol). Local anesthetics and a short acting narcotic produced significantly less effects. (Journal abstract modified)

194749 Garner, Lawrence L.; Wang, Richard I. H.; Hieb, Elizabeth. Department of Ophthalmology, VA Center, Wood, WI **Comments on treatment: eye changes following phenothiazine administration.** Wisconsin Medical Journal. 73(9):119-121, 1974.

The effects of phenothiazine on vision were reported. Phenothiazines which have been most strongly linked to significant ocular changes include chlorpromazine, thioridazine, fluphenazine and trifluoperazine. Major sites of ocular changes following phenothiazine administration include the retina, conjunctiva, cornea, and lens. Patients who experess symptoms may complain of blurred vision, problems in reading or doing close work, and reduced peripheral vision. Therepeutic guidelines are included.

195443 Greenwood, M. H.; Friedel, J.; Bond, A. J.; Curzon, G.; Lader, M. H. De Crespigny Park, Institute of Psychiatry, University of London, London, S.E.5, England **The acute effects of intravenous infusion of L-tryptophan in normal subjects.** Clinical Pharmacology and Therapeutics. 16(3,Part1):455-464, 1974.

The effects of intravenous infusion of L-tryptophan at doses of 75 and 100mg/kg were compared with that of normal saline in healthy volunteers by means of a series of psychological and physiological measures. The 100mg/kg infusion produced a 40 fold increase in free tryptophan and an eight fold increase in the bound form. Few of the objective tests showed any differences. The electroencephalogram showed a significant in-

crease in slow wave activity and a trend toward decreased fast wave activity. Some impairment of a motor speed task was also noted. Reduction of arousal and increased drowsiness (but no euphoria) were shown by the subjective ratings. 46 references. (Author abstract)

195444 Hillestad, L.; Hansen, T.; Melsom, H.; Drivenes, A. Medical Departments, Sentralsykehuset, Akershus, Oslo, Norway **Diazepam metabolism in normal man: I. Serum concentrations and clinical effects after intravenous, intramuscular, and oral administration.** Clinical Pharmacology and Therapeutics. 16(3,Part1):479-484, 1974.

In a study of diazepam metabolism in man, it was demonstrated that serum concentrations obtained by administration of diazepam to normal subjects are dependent on the mode of administration. After intravenous injection the maximal level of about 1600ng per milliliter was reached in 15 minutes. Oral and intramuscular administration were followed by maximal levels of about 490ng per milliliter in 30 minutes and of 290ng per milliliter in 60 minutes, respectively. The clinical effects exhibited an accurate relationship to the serum concentration levels. At high levels of diazepam in the serum, the sedative effect was accompanied by a marked deterioration of several mental functions and coordination. Acute administration of single doses of diazepam did not produce significant amounts of the metabolite, N-desmethyldiazepam, which therefore was unlikely to have contributed to the clinical effects. 10 references. (Author abstract)

195847 Vohra, J. K. Cardiac Dept., Royal Melbourne Hospital, Melbourne, Vic. 3050, Australia **Cardiovascular abnormalities following tricyclic antidepressant drug overdosage.** Drugs (Basel). 7(5):323-325, 1974.

Cardiovascular abnormalities following tricyclic antidepressant drug (TAD) overdosage were examined over an 18 month period in patients admitted to the Royal Melbourne Hospital. The metabolism of the TAD overdosage is discussed. Some 50% to 60% of the patients consumed small amounts of the drug and presented no problems of medical management. Those who did present problems were infants, children and those receiving antihypertensive therapy with catecholamine depleting drugs such as guanethidine. Cardiovascular side-effects and mechanisms of action are described. Drug therapy and other supportive treatment are discussed. 11 references.

196923 Monov, A.; Petkov, V. no address /**Acute intoxications with neuroleptics.**/ Ostri otravyaniya s nevroleptitsi. Savremenna Medicina (Sofia). 24(10):18-22, 1973.

A group of 160 patients with acute intoxication with neuroleptics (phenothiazines, benzodiazepines, or reserpine like drugs) in combination with barbiturates, antidepressants, or quinine was studied. Patients were divided into three groups depending on the severity of their symptoms, and cerebral syndrome was found to be common to all three. Toxic encephalopathy with Meniers like syndrome was present in the mild form of intoxication. The moderate form of intoxication included symptoms of somnolency, shock, and stupor. Coma and deep coma with areflexia were present in the severe and extreme severe forms. Phenothiazines commonly induced hypotension and tachycardia; quinine, imipramine, and bellergamin induced mydriasis; and barbiturates most often affected conscious processes. 7 references. (Journal abstract modified)

197029 Persson, G. Dept. of Psychiatry, Sahlgren's Hospital, S-413 45 Gothenburg, Sweden **Plasma lithium levels and side effects during administration of a slow release lithium sulphate preparation (lithium lipett C) and lithium carbonate levels.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(2):174-182, 1974.

The effects of lithium lipett C, a new lithium sulfate preparation with slow release (90% of the lithium content within less than 4 hours) were compared with the effects of lithium carbonate tablets. In spite of a swift release, there was a smoother plasma lithium curve with the lipett C than with the carbonate tablets. The frequency of the side-effect diarrhea with the lipett C administered twice a day was higher than with carbonate tablets administered three or four times a day and similar to that with slower releasing lithium sulfate lipett. The diarrhea was probably caused both by the effect of the lithium ion on distal parts of the intestinal canal and by the sulfate ion. The frequency of the other side-effects was similar to that of the lipett C and the carbonate tablets. The advantages of the lipett C were counteracted by the drawbacks of the side-effects. 8 references. (Author abstract modified)

197539 Woody, George E.; O'Brien, Charles P. Drug Dependence Treatment Center, Philadelphia VA Hospital, Philadelphia, PA **Anticholinergic toxic psychosis in drug abusers treated with benztropine.** Comprehensive Psychiatry. 15(5):439-442, 1974.

Six case descriptions of toxic psychosis occurring in heroin addicts prescribed benztropine are reported. Four patients overmedicated themselves with benztropine; two others developed toxic psychosis while on a normal dose. Two conclusions are drawn: 1) that the tendency of drug abusers to overmedicate themselves can cause toxic psychosis when anticholinergics are prescribed, and 2) that heroin addicts may be unusually sensitive to an anticholinergic toxic psychosis. 7 references. (Author abstract)

198044 Phillips, John. Tulane Medical School, New Orleans, LA **Potential cardiotoxicity from phenothiazines and tricyclic antidepressants.** Psychopharmacology Bulletin. 10(2):9-10, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which evaluated the cardiotoxicity of phenothiazines and tricyclic antidepressants. These agents may produce ST and T-wave abnormalities in the elctrocardiogram of the experimental animal and in larger doses they may produce tachyarrhythmias and various forms of heart block. It is suspected that various rhythm disturbances, conduction disturbances, and even sudden death may occur with the use of these agents in commonly acceptable therapeutic dosages and also that cardiomyopathies may be produced by such usage, leading to cardiac enlargement and the usual manifestations of congestive heart failure. These agents may also speed cellular aging. However, the true physiologic significance of the electrocardiographic changes that are commonly seen in humans is not known. (Journal abstract modified)

16 METHODS DEVELOPMENT

193073 Blumenthal, David S.; Burke, Robert; Shapiro, Arthur K. Special Studies Laboratory, Payne Whitney Clinic, New York Hospital - Cornell University Medical College, New York, NY 10021 **The validity of 'identical matching placebos'.** Archives of General Psychiatry. 31(2):214-215, 1974.

A laboratory simulation of the double-blind clinical study in which inactive control drugs are described as 'identical matching placebos', is reported. For five of six drug categories, subjects simulating experimenters or patients significantly differentiated active drug from placebo based on physical

characteristics of the medications. Thus, many of the identical matching placebos were not in fact identical but were different from the active drug in physical properties such as texture, color, and thickness. The results suggest that the assumption that 'identical matching placebos' as used in a study should be tested by preliminary comparison of the placebo with the active drug. Major recommendations are that active drug and control be administered as capsules, that research assistants be minimally aware of the experimental design of the study, that the Federal Drug Administration or National Institutes of Health formulate standard capsules for use in controlled clinical evaluation studies, and that the placebo contain active ingredients to mimic the side-effects of the active drug. 12 references. (Author abstract)

194561 Park, George Bennet. University of Kansas **The application of electroanalytical techniques to biochemical systems. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-12610 HC$12.50 MF$4.00 141 p.

Voltammetry and chronocoulometry were applied to problems in neurochemistry, pharmacology and clinical chemistry. A new method for the analysis of uric acid using chronocoulometry is described which requires no sample preparation, no reagents, and the uric acid concentration is read out digitally in 4 seconds. The protective system of the brain toward catecholamines was studied and substantiated in vitro by electrochemically following the air oxidation of norepinephrine, dopamine and 6-hydroxydopamine with and without the presence of rat brain slices. The possible protective capacity of ascorbic acid, glutathione, acetylcholine, serotonin, and superoxide dismutase was also studied. Brain tissue and ascorbic acid are shown to protect catecholamines for long periods of time but are shown to have little or no effect on the rate of air oxidation of 6-hydroxydopamine at physiological pH. A preliminary study of the utility of electrochemical methods of analysis for phencyclidine and LSD is presented. (Journal abstract modified)

196776 Slanska, J.; Benesova, O. Institute of Pharmacology, Prague 10, Srobarova 50, Czechoslovakia **Personality trait stability-lability and its significance for pharmacological research.** Activitas Nervosa Superior (Praha). 16(2):119-121, 1974.

Research concerning personality trait stability - lability with physostigmine (Phs) was reported at the 11th Interdisciplinary Conference on the Experimental and Clinical Study of Higher Nervous Functions (Piestany, November 1973). No difference in the reaction to Phs was found between personality groups in the results of the Abramson-Jarvik body inventory and only small ones in the results of attention tests. However, more complicated tests detected significant differences between stable and labile Ss. In both tests, Phs impaired the performance of labile probands. The results indicated interesting differences between stable and labile Ss after placebo administration in recall 24 hours after acquisition. The experiment indicates that the performance after both Phs and placebo are highly dependent on personality trait stability - lability and on the type of difficulty of the test situation. These facts should be respected when selecting Ss for research, especially in clinical trials of new drugs. 6 references.

198042 Turner, David A.; Purchatzke, Gerald; Gift, Thomas; Farmer, Carol; Uhlenhuth, E. H. Department of Psychiatry, University of Chicago, Chicago, IL **Intensive design in evaluating anxiolytic agents.** Psychopharmacology Bulletin. 10(2):7-8, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which showed the usefulness of intensive design in detecting the effects of an established antianxiety agent in a single patient. Patients were predominantly anxious, with a primary diagnosis of psychoneurosis and psychoneurotic personality disorder or adult situation reaction. The medications were diazepam, 5mg three times daily, and a matching placebo. The patient rated himself weekly on a list of 71 common psychoneurotic symptoms and on global scales of current status and change since the last session. Individual patients discriminated diazepam from placebo on a number of measures. Reaction times and compulsiveness were greater with diazepam than with the placebo, but other effects favored diazepam over placebo. This experimental design appears capable of detecting the effects of antianxiety agents. (Journal abstract modified)

17 MISCELLANEOUS

193035 Boston Collaborative Drug Surveillance Program; Jick, Hershel. 400 Totten Pond Rd., Waltham, MA 02154 **Amphetamines and malignant lymphoma.** Journal of the American Medical Association. 229(11):1462-1463, 1974.

The relationship of exposure to amphetamines and malignant lymphoma was evaluated using data collected by the Boston Collaborative Drug Surveillance Program. Of the 315 patients with this diagnosis, none gave a history of exposure to amphetamines, while among 38,900 control subjects 218 gave such a history. The findings do not lend support to the recently published hypothesis of an association between amphetamine usage and Hodgkin disease. 4 references. (Author abstract)

193192 Greenblatt, David J.; Shader, Richard I. Mass. General Hospital, Boston, MA 02114 **Rational use of psychotropic drugs. II. Antianxiety agents.** Journal of the Maine Medical Association. 65(9):225-229, 1974.

The use of psychotropic drugs as antianxiety agents is reported. Topics discussed include choice of antianxiety agent, barbiturates, propanediols, antihistamines, antidepressants, benzodiazepines, major tranquilizers, and beta-adrenergic antagonists. It is noted that since anxiety is an episodic disorder, drug therapy is most rational when coinciding with exacerbation of symptoms. The necessity to titrate drug dosage is emphasized. 44 references.

194054 Fields, Rona M. no address **A society on the run: a psychology of Northern Ireland.** Middlesex, England, Penguin Education, 1973. 216 p. 50 p.

A psychological view of the tragic civil disorder in Northern Ireland is presented. Use of drugs in detention camps is described, including the use of librium to diminish sexual potency.

194066 Tyrer, Peter. South Block, Southampton General Hospital, Southampton S09 4XY, England **The benzodiazepine bonanza.** Lancet (London). 2(7882):709-710, 1974.

The pharmacological properties of 1,4-benzodiazepines, including Six other benzodiazepine compounds are cited, and librium and valium, are discussed. The testing of at least four other benzodiazepines is previewed. Metabolic pathways of benzodiazepines are illustrated, noting small differences between individual compounds of benzodiazepines. Despite clinical and pharmacological similarity, the medical profession and pharmaceutical industry are cautioned to reexamine benzodiazepines, particularly in that the introduction of some new benzodiazepines results in no clinical advance. 17 references.

194407 Johnson, D. A. W. Crumpsall Hospital, Manchester, MS 6RB, England **A study of the use of antidepressant medication in general practice.** British Journal of Psychiatry (London). 125:186-192, 1974.

An analysis of the treatments prescribed to three different groups of patients suffering from depression suggests that psychotropic drugs are often used inappropriately in general practice. This view was confirmed by a survey of general practitioners. Reasons for drug defaulting by patients are also explored. It is suggested that in the setting of urban general practice the potential for the traditional family doctor relationship with patients is limited and his knowledge of psychiatry and experience with psychotropic drugs are relatively small. 11 references. (Author abstract)

194409 Ballinger, Brian R.; Simpson, Elliott; Stewart, Michael J. Royal Dundee Liff Hospital, Liff, by Dundee, Scotland **An evaluation of a drug administration system in a psychiatric hospital.** British Journal of Psychiatry (London). 125:202-207, 1974.

The reliability of drug administration to psychiatric inpatients following the introduction of a new drug administration system is assessed. The urines of 236 patients were tested for various psychotropic drugs. In 6.4% of patients, prescribed drugs were not detected, in 10.2% nonprescribed drugs were detected, and in four patients both discrepancies were present. The relationships between these discrepancies and certain characteristics of the patients and drugs are discussed. Possible causes of these findings include nurse error, patient noncooperation; laboratory error and abnormalities of metabolism. The inpatients in a mental subnormality hospital were also investigated, and discrepancies were found both before and after introduction of the new system. 16 references. (Author abstract)

194559 Ramachandra, K.; Ramachandran, T. Madras Medical College, Madras-3, India **Psychotropic drugs.** Antiseptic (Madras). 69(3):185-189, 1972.

Psychotropic drugs are categorized according to their psychological effects. Drugs for psychoses, anxiety, depression, and psychotomimetic drugs are discussed. Toxic reactions of phenothiazines are outlined. Drugs for treatment of depression included caffeine, amphetamine, phenmetrazine, methylphenidate and pipradol.

195240 Lullmann, Heinz; Ziegler, Albrecht. Institut fur Pharmakolgie, Universitat Kiel, D-2300 Kiel, Germany **A transient state concept of drug receptor interaction.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 280(1):1-21, 1973.

A transient state concept of drug receptor interaction is discussed. Experimental results obtained with muscarine like drugs cannot be explained satisfactorily by existing drug receptor theories. The time courses and extents of the negative inotropic effects and that of the desensitization caused by cholinomimetic drugs were recorded in guinea-pig isolated, electrically driven atria. The uptake of 3H-carbachol by the tissue was measured under identical experimental conditions. A concept of drug receptor interaction is proposed based upon these experimental results. It differs from the existing theories by including both the disposal of the drug molecules in the biphase (drug transport) and the existence of an inactivated drug receptor complex. The active drug receptor complex is regarded as a transient state. The transient state concept makes it possible to use only one set of constants to describe uptake curves and effect curves over the entire dose range. 56 references. (Author abstract)

195925 Snyder, Solomon H. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD **Mechanism of antidepressant efficacy of monoamine oxidase inhibitors: inhibition of monoamine oxidase or of catecholamine reuptake.** Journal of Psychiatric Research (Oxford). 10(2):153, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,the mechanism of antidepressant efficacy of monoamine oxidase (MAO) inhibitors was discussed. Several MAO inhibitors were mentioned; tranylcypromine was said to be the most effective antidepressant of the MAO inhibitors. The practical and the theoretical importance of a clinical evaluation of tranylcypromine were examined. Studies of the effects of various drug isomers upon catecholamine uptake by norepinephrine and dopamine neurons in both the central and peripheral nervous systems were said to have clarified the mechanisms regulating amine uptake with a variety of possible therapeutic implications. The contrasting stereochemical requirements for psychedelic and central stimulant effects of amphetamine analogs were seen as having great theoretical interest. (Journal abstract modified)

195926 Mandell, Arnold J.; Knapp, Suzanne. Department of Psychiatry, University of California at San Diego, La Jolla, CA **The multiplicity of interactions of psychotropic drugs with the brain serotonin biosynthetic unit.** Journal of Psychiatric Research (Oxford). 10(2):153-154, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,a study was discussed which, using subcellular fractions, systematic regional studies, and a variety of assay techniques, demonstrated two forms of the rate limiting enzyme in the biosynthesis of serotonin in rat brain: soluble and particulate tryptophan hydroxylase. After a description and evaluation of the study, it was concluded that the measurement, time, and dose phenomena observable when the two forms of the enzyme are maintained and individually studied (simultaneously) go a long way toward resolving the conflicts in the literature about alterations in serotonin biosynthesis in response to psychotropic drugs. (Journal abstract modified)

195933 Gruenberg, Ernest M.; Fieve, R.; Turns, Danielle. New York State Psychiatric Institute, New York, NY **Does lithium in drinking water prevent mental disorder?** Journal of Psychiatric Research (Oxford). 10(2):158, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,studies relating to lithium as a therapeutic and prophylactic agent in the treatment and prevention of mental disorders were discussed. It was theorized that if higher lithium concentration in drinking water can prevent coronary arteriosclerosis it may also prevent cerebral arteriosclerosis. It was concluded that testable hypotheses which would help evlaute the implied chain of inference need to be developed. 4 references. (Journal abstract modified)

195935 Shagass, Charles; Straumanis, John J.; Overton, Donald A. Temple University Medical Center, Phildelphia, PA **Somatosensory evoked response wave shape stability: relationships to psychiatric diagnosis and effects of psychoactive drugs.** Journal of Psychiatric Research (Oxford). 10(2):159-160, 1974.

In a paper presented at the Meeting of the Psychiatric Research Society, October 20 and 21, 1972, in Washington, D.C.,data dealing with wave shape stability of somatosensory responses in various psychiatric disorders was reported. The findings were: (1) chronic paranoid and undifferentiated schizophrenics have greater stability from 15 to 100msec after stimulus than normals, acute or borderline schrophrenics or nonpsychotic patients; and (2) manic patients have less stability from 15 to 100msec than matched nonpatients. Tests of patients while on lithium, amitryptyline and phenothiazine therapy failed to demonstrate significant shifts in wave shape stability. It was suggested that the greater stability found in chronic schizophrenics may be a manifestation of 'restricted dynamic range of cerebral responsiveness', and that tonic hyperactivity of subcortical areas, such as the septal region, which may modulate cortical responses, could be one possible mechanisms leading to dynamic range restriction. (Journal abstract modified)

195936 Klein, Donald F. Long Island Jewish Hillside Medical Center, Department of Psychiatry, Glen Oaks, NY **Interactive prediction of drug induced change.** Journal of Psychiatric Research (Oxford). 10(2):160, 1974.

In a paper presented at the Meeting of the Psychiaric Research Society, October 20, and 21, 1972, in Washington, D.C.,the question of the prediction of drug induced change in mental patients was discussed. The two general approaches to predictions and problems with these methods were reviewed, and an approach to the prediction problem by a method that specifically searches for interactions and uses simple psychopathological items such as criterion measures was suggested. A procedure which uses a contextual modifier routine was briefly described. (Journal abstract modified)

196031 L'Etang, Hugh. Practitioner, 5 Bentinck Street, London W1M 5RN, England **Psychiatric illness and the future of nations.** Proceedings of the Royal Society of Medicine (London). 67(7):619-621, 1974.

Psychiatric illness in heads of state is discussed. The study of such history is recommended because: it reveals something of the psychological and psychiatric background of world leaders; it may reveal some idea of the psychological reactions between world leaders; and it may warn the public about the effects of medical treatment on leaders. It is felt that the effect of drugs, even the common every day drugs for travel sickness or respiratory infection, on the leader and on decision-making is a sadly neglected problem. Several examples of modern leaders who took various types of medication, including tranquilizers, benzedrine, and steroids, are discussed. 13 references.

196034 Berner, P.; Kryspin-Exner, K.; Poeldinger, W. Psychiatrische Univ.-Klinik, Lazarettgasse 14, A-1097, Vienna, Austria **Therapy possibilities for therapy-resistant depressions.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 7(4):189-193, 1974.

Therapy possibilities for therapy resistant depressions are examined. Cases are labeled as therapy resistant if the patient did not react satisfactorily after being treated for 3 weeks by two different types of antidepressants. The following treatments are discussed: electroconvulsive therapy; interruption of all therapy; infusion; the combination of dimethyl and monomethyl derivatives of tricyclic antidepressants in alternating form; intensive therapy with neuroleptics; and the use of monoamine oxidase inhibitors. 7 references.

196035 Ginestet, D. Service Hospitalo-Universitaire de Sante Mentale et de Therapeutique, 100 rue de la Sante, F-75674 Paris-Cedex 14, France **The psychiatrist attitudes and therapeutic means when faced with resistant depressions.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 7(4):194-198, 1974.

Psychiatrist's attitudes and therapeutic means when faced with resistant depressions are examined. Resistant depressions are seen as those in which a total or partial resistance of the

depressive vital syndrome occurs after a tricyclic treatment. It was found that the amount of chemotherapy resistant depressions remains important, especially the unipolar forms and schizophrenic depressions. Fear of suicide leads the psychiatrist to use electroshock therapy. New possibilities for treatment are offered. The use of new compounds, L-Dopa, thyrotropin releasing hormone or 5-HTP, to cure depressions or in the prevention of depression through use of lithium salts was discussed. Neurotic depressions are the most difficult to resolve, especially the hypochondriac forms. Sismotherapy is not indicated. Antidepressants and psychotherapy yield haphazard results and the hospitalization system tends to chronicize the patients. It is felt that a biological background of mood disorders is behind some of the resistant forms of depression. 13 references. (Author abstract modified)

196036 Kelly, Desmond. St. George's Hospital Medical School, Atkinson Morley's Hospital, 31 Copse Hill, GB-London, S.W. 20, England **Treatment of resistant depression.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 7(4):199-204, 1974.

The treatment of resistant depression is discussed. Resistant depression implies failure to respond to an adequate dosage of tricyclic antidepressants, possibly followed by a monoamine oxidase inhibitor and a course of electroconvulsive therapy (ECT). Three types of treatment are advocated for resistant depression: combined tricyclic antidepressant and a monoamine oxidase inhibitor; modified narcosis combined with ECT and antidepressants; and psychosurgery. The benefits and possible drawbacks and side-effects of the treatments are discussed fully. 12 references. (Author abstract modified)

196037 Hamilton, M. Dept. of Psychiatry, Univ. of Leeds, 15 Hyde Terrace, Leeds LS2 9LT, England **Drug resistant depressions: response to E.C.T.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 7(4):205-206, 1974.

The response to electroconvulsive therepy (E.C.T.)by drug resistant depressions was examined in a group of patients. Ss were randomly allocated to treatment by either imipramine or phenelzine for from 4 to 8 weeks. If at that time, the reduction in symptoms was trivial, Ss were transferred to a course of E.C.T.,consisting of six to 12 treatments. The response to treatment by E.C.T. after imipramine had failed was significantly worse than the response to E.C.T. as a primary treatment. This was not true when the primary treatment was phenelzine. It is suggested that E.C.T. produced results through a mechanism related to the action of imipramine but not that of phenelzine. 1 reference. (Author abstract modified)

196038 Walcher, W. Psychiatrisch-Neurologische Universitatsklinik, Auenbruggerplatz 22, A-8036, Graz, Austria **Influence-possibilities on therapy-resistant late depressions.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 7(4):207-210, 1974.

Influence possibilities on therapy resistant late depressions are discussed. The treatment of 64 patients admitted to the hospital with this diagnosis who ranged in age from 53 to 92 years old is described. All Ss showing signs of organic disorder or disturbances of cerebral blood supply underwent intensive heart treatment; in retarded cases with signs of stupor, an appropriate infusion and substitution treatment was carried out under laboratory conditions; those with mental confusion due to arteriosclerotic and/or antidepressive medication were sedated beside a heart - hemodynamic and infusion treatment with only minor tranquilizers; patients with continued agitation or anxiety were administered base neuroleptics with mild thymoleptic effect; in cases with chronic motive insufficiency and total inactivity, infusions with monochlorimipramine were administered; Ss with depressive paranoic symptoms and vegetative somatic signs reacted well to depot fluphenazine or depot fluanxol; and psychotherapy and postclinical treatment were seen to be important in the treatment of late depression. (Author abstract modified)

196040 Levine, J.; Raskin, A. Room 9-105, NIMH, 5600 Fishers Lane, Rockville, MD 20852 **Predicting treatment responsiveness-resistiveness in a population of depressed patients.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuggart). 7(4):217-222, 1974.

Predictors of treatment resistance or responsiveness were identified in the analysis of a multihospital collaborative study. Many variables were included and representative drugs from the tricyclic, neuroleptic, anxiolytic and monoamine oxidase inhibitor classes were evaluated for their effect on treatment outcome. Imipramine and chlorpromazine were the only drug conditions which, when combined with the other predictor variables such as marital status, showed a significant effect on the outcome. Although the combination of variables was shown to be statistically significantly related to outcome, the strength of the prediction was small and accounted for only 10% of the variance. Bipolar and unipolar distinction and certain biochemical measurements are not included. 1 reference. (Author abstract modified)

196231 Markoff, Richard A.; Kinzie, J. David; Botticelli, Max G.; Bolian, George C. Honolulu, HI **A simplified guide to the rational use of psychotropic drugs.** Hawaii Medical Journal. 33(6):201-206, 1974.

Since a great deal of psychiatric primary care is rendered by nonpsychiatric physicians, and considerable use must be made of psychotropic medications in the process, a method for making appropriate choices among psychotropic medications is presented. However, a number of difficulties attend this area of practice. There are many psychotropic drugs and it is often hard to differentiate them clearly in terms of actions and indications. In addition to being somewhat imprecise, psychiatric nosology is sometimes less than ideally relevant to questions of choice of therapeutic agent. 12 references. (Author abstract)

197269 Wheatley, David. no address **Psychopharmacology in medical practice.** New York, Appleton-Century-Crofts, 1973. 200 p. $12.50.

Fourteen years of clinical psychopharmacological research by the General Practitioner Research Group in England is summarized. Throughout, attention is paid to the practitioner as the frontline person in treatment intervention for mentally ill citizens. As anxiety and depression are the predominating symptoms of mental illness that the general practitioner generally treats, drugs that are clinically useful in the management of these particular symptoms are emphasized. Contemporary issues in psychopharmacology are considered, notably patient - professional factors influencing drug response, side-effects, methodological problems in assessing treatment efficacy in outpatients, and transcultural aspects.

197276 Niskanen, Pekka; Achte, Kalle A. Psychiatric Clinic, Helsinki University Central Hospital, Helsinki, Finland **The course and prognosis of schizophrenic psychoses in Helsinki: a comparative study of first admissions in 1950, 1960 and 1965.** Helsinki, Psychiatric Clinic, Helsinki Univ. Cent. Hosp., 1972. 56 p.

The 5 year outcome of three cohorts of schizophrenic patients is reported, one admitted during the predrug era and two admitted after the introduction and widespread use of the antipsychotic drugs. The basic findings are that the three cohorts of patients did not differ significantly in terms of symptoms, social recovery, or number of readmissions at 5 year followup. The 1965 patients were significantly less often in hospitals at 5 years and had shorter hospitalizations than the patients in the 1950 and 1960 groups, attributable to the increased availability of partial hospitalization, outpatient services, and rehabilitation programs, and to changing public attitudes. The study would indicate that the antipsychotic drugs have not affected long-term social recovery in schizophrenia.

197534 van Praag, H. M. Dept. of Biological Psychiatry, Psychiatric University Clinic, State Univ. of Groningen, Groningen, The Netherlands **New developments in human psychopharmacology.** Comprehensive Psychiatry. 15(5):389-401, 1974.

Notwithstanding the absence of spectacular new therapeutic possibilities, a number of promising new developments in psychotropic drug research are described according to three broad divisions: (1) biological psychiatry, (2) neuroendocrinology and (3) pharmacokinetics. In the past, psychotropic drugs have been prescribed according to the 'cookbook principle.'However, it is expected that the rapid expansion of therapeutic applications will increasingly necessitate knowledge of biological determinants of disturbed behavior, both in order to practice pharmacotherapy on a professional level and in order to be able to follow and evaluate new trends, a factor which should be taken into account in the education and training of psychiatrists. 32 references. (Author abstract modified)

197676 Waldmeier, P. C.; Maitre, L. Research Department, Pharmaceuticals Division, Ciba-Geigy Ltd., CH-4002 Basel, Switzerland **3,4-Dihydroxyphenylacetic acid (DOPAC): a possible endogenous inhibitor of indoleamine-N-methylation in the rat brain.** Experientia (Basel). 30(5):456-458, 1974.

The effects on indoleamine-N-methylation of two well established neuroleptics and of the two endogenous amine metabolites whose concentrations in the brain are most spectacularly increased by the former were studied. The whole brains of 50 male albino rats were used. The two neuroleptics used, chlorpromazine and clozapine, had no influence on tryptamine methylation up to concentrations of .0001 M and .001 M, respectively. 3,4-Dihydroxyphenylacetic acid (DOPAC), and 3-methoxy-4-hydroxyphenylacetic acid (HVA), inhibited tryptamine methylation to varying degrees depending on the concentration applied. The inhibitory capacity of DOPAC was two to three times greater than that of HVA. Considering that neuroleptics increase the concentration of endogenous DOPAC enormously, it is felt that the antipsychotic activity of these drugs may be related to the rise in the intraneuronal content of DOPAC acting as a methylation regulator. 16 references.

198048 Balter, Mitchell B.; Bauer, Mary Lou. Psychopharmacology Research Branch, NIMH, Rockville, MD **Psychotherapeutic drugs: studies of usage patterns and studies of prescribing practices.** Psychopharmacology Bulletin. 10(2):12, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which included data sources for a project on the nature and extent of psychotherapeutic drug usage and the prescribing practices of private physicians. Sources include: a national survey of drug acquisition and use; a cross-national study of antianxiety/sedative drug use based on nationwide household surveys in each of nine European countries; special analyses of data from the National Prescription Audit of Gosselin and Company on prescriptions filled in drugstores; and a 3 month sample survey of all prescriptions written by a panel of physicians in the Gosselin Audratrex reporting system. Sources where results of these surveys may be found are included. 3 references. (Journal abstract modified)

198049 Hesbacher, Peter; Rickels, Karl. Private Practice Research Group, Philadelphia General Hospital, Philadelphia, PA **Survey of health and illness in family practice.** Psychopharmacology Bulletin. 10(2):13-14, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which provided information about the detection and treatment of psychiatric illness, from a survey of seven family physicians' practices. A standardized psychiatric assessment of the severity of psychiatric disturbance was conducted by the same psychiatrist for a subset of patients in five of the seven practices. The treating physician made an Overall Judgment of Psychopathology according to a seven patient point scale, and the patient rated himself for 35 common psychoneurotic complaints from the Patient Symptom Checklist. Data were analyzed to provide information about five topics: illness detection in the family practice; social factors that influence psychiatric symptomatology; the use of psychotropic drugs; the relationship of psychotropic drug use to designated emotional illness; and a determination of whether clinical trial patients are representative of emotionally ill patients in these practices. (Journal abstract modified)

198050 Swett, Chester, Jr. Boston Collaborative Drug Surveillance Program, Boston University Medical Center, Boston, MA **Patterns of chlorpromazine use in general and psychiatric hospitals.** Psychopharmacology Bulletin. 10(2):14, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which identified the patterns of chlorpromazine use in general and psychiatric hospitals. The mean age of 556 medical patients who received chlorpromazine was 54.6years, and the most common primary diagnosis was neoplastic disease; anxiety was the most common indication for drug use. Adverse reactions attributed to the drug use were reported in 68 patients. In 470 psychiatric patients, the mean age was 36.4years, and the most common diagnosis was schizophrenia; thought disorder was the common indication for drug use. Adverse reactions were reported in 150 patients. Reactions were more frequent with higher daily doses, and the parenteral route was associated with an earlier onset of a reaction in both hospital settings. 1 reference. (Journal abstract modified)

198051 Tracy, Martha; Shader, Richard I. Psychopharmacology Research Laboratory, Harvard Medical School, Boston, MA **Drug use patterns among the elderly.** Psychopharmacology Bulletin. 10(2):14-17, 1974.

At the Early Clinical Drug Evaluation Units' Meeting in May 1973, a paper was presented which surveyed medication use by patients over the age of 65 in the U.S. Ss were 87 healthy volunteers, 337 nursing home residents, and 130 psychiatric inpatients. The mean number of drugs used per capita was 1.8drugs per person per day for the geriatric volunteers and 3.9and 2.5drugs for the nursing home residents and psychiatric inpatients. Multiple vitamins were taken most frequently by the volunteer population. Psychotropic agents were the most frequently used class by each of the other

groups. The most frequent combinations were multiple vitamins with cardiovascular agents for the volunteer population, psychotropic drugs with sedative hypnotics for the nursing home population, and psychotropic drugs with diuretics for the psychiatric inpatients. (Journal abstract modified)

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